A DISSERTATION ON

"THE ROLE OF CT PERFUSION IN THE CHARACTERISATION OF SOLITARY RENAL LESIONS – AN ADDED VALUE TO MULTIPHASIC CT"

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CERTIFICATE

This is to certify that the dissertation titled **"THE ROLE OF CT PERFUSION IN THE CHARACTERISATION OF SOLITARY RENAL LESIONS – AN ADDED VALUE TO MULTIPHASIC CT"** submitted by **Dr.SWARNALAKSHMI.S,** appearing for **M.D.RADIODIAGNOSIS** degree examination in May 2018, is a bonafide record of work done by her, under my guidance and supervision in partial fulfillment of requirements of The Tamilnadu Dr. M.G.R Medical University, Chennai. I forward this to The Tamilnadu Dr. M.G.R Medical University, Chennai.

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DECLARATION

I, **Dr. SWARNALAKSHMI.S,** certainly declare that this dissertation titled, "**THE ROLE OF CT PERFUSION IN THE CHARACTERISATION OF SOLITARY RENAL LESIONS – AN ADDED VALUE TO MULTIPHASIC CT**", represent a genuine work of mine, done at the Barnard Institute of Radiology, Madras Medical College and Rajiv Gandhi Government General Hospital, under the supervision of **Prof.D.RAMESH, M.D.R.D**., Professor, Barnard Institute of Radiology, Madras Medical College and Rajiv Gandhi Government General Hospital.

I, also affirm that this bonafide work or part of this work was not submitted by me or any others for any award, degree or diploma to any other university board, neither in India or abroad. This is submitted to The Tamil Nadu Dr.MGR Medical University, Chennai in partial fulfillment of the rules and regulations for the award of M.D Degree in Radiodiagnosis (Branch VIII).

Date :

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Dr.SWARNALAKSHMI.S

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Introduction

"THE ROLE OF CT PERFUSION IN THE CHARACTERISATION OF SOLITARY RENAL LESIONS – AN ADDED VALUE TO MULTIPHASIC CT"

1. INTRODUCTION

Majority of the renal lesions are found incidentally by routine ultrasound examination. And in recent times, the diagnosis of renal masses have increased, because of the widespread use of computed tomography (CT), and magnetic resonance (MR) imaging.

Most of the lesions turn out to be simple renal cysts which can be diagnosed easily and they do not require any treatment. However, solid and complex cystic renal masses are also found, and most of them are clearly malignant which needs prompt surgical removal, although some may be benign and surgery may not be needed in such cases.

Thereby, the proper characterisation of the renal masses is needed for appropriate management and helps in deciding the need for surgery.

There have been many studies focussing on the imaging features and degree of enhancement on multiphasic, multidetector CT or MRI as a means of distinguishing benign and malignant renal lesions and also there have

been reports of subtype differentiation of renal cell carcinomas by CT or MRI[1,2,3].

Although the great value of imaging for detection of renal lesions has increased in recent years, the accuracy rate on preoperative characterisation of their nature remains low[4]. Percutaneous biopsy could be a useful tool in dubious cases, but it is an invasive approach[5,6].

Recently, computed tomography perfusion (CTp), a functional tool which allows a quantitative evaluation of tissue perfusion through consecutive scans acquired during contrast media injection, showed promising results in the oncologic field, even in renal lesion characterisation[7] and further aids in subtyping of renal cell carcinomas.

Perfusion CT is based on the temporal changes in tissue attenuation after intravenous administration of iodinated contrast media. Tissue iodine concentration determines enhancement and is an indirect reflection of tissue vascularity and vascular physiology[8,9]. These are predicted based on certain perfusion parameters, namely blood flow (BF), blood volume (BV), mean transit time (MTT) and permeability (PMB).

Rationale of the study

2. RATIONALE OF THE STUDY

Most of the renal tumours (almost ninety percent) come under five histologic categories: clear cell carcinoma (or conventional carcinoma), which is the most common, chromophobe carcinoma, papillary carcinoma, and two common benign tumours, namely angiomyolipoma and Oncocytoma[10].

Angiomyolipoma (AML) is a common benign tumour of the kidney and presence of intratumoral fat allows accurate identification by imaging.[11,12] But, in cases of AML with minimal fat, intratumoral fat cannot be visualized in an AML on routine imaging[13-15]. And they resemble renal cell carcinoma (RCC), leading to surgery unnecessarily. Also differentiating between oncocytoma and renal cell carcinoma represents a diagnostic challenge[4].

Renal cell carcinomas (RCC) account for 80–90% of all renal neoplasms,[1,2,16] with multiple subtypes that differ in their histopathologic features, genetic expression pattern, and clinical behaviour. Among the renal cell carcinomas, Clear cell RCC, papillary RCC and chromophobe RCC are the most representative subtypes, accounting to 65–70%, 15–20%, and 6–11% of RCCs, respectively[3,17].

Different histopathologic entities show different prognosis and biologic behaviour, and also differ in their response to the available treatment options[18,19]. Because of this, accurate subtyping of RCC by imaging becomes

important for optimising treatment protocols and also for predicting the prognosis[20].

The identification of renal lesion type, firstly discriminating between malignant and benign, could represent an important diagnostic goal in order to choose the best management.

For example, diagnosis of RCC at an early stage means a less invasive therapeutic approach and has a better prognosis, whereas unnecessary surgical interventions could be avoided in case of accurate identification of benign lesions.

While contrast enhanced computed tomography (CECT) provides information on the size, morphology and response assessment in renal cell carcinomas, a newer imaging technique like perfusion CT provides new perspectives in imaging of RCC.

Perfusion CT depicts regional tumour perfusion and vascular permeability which are indirect parameters of tumour angiogenesis and thereby provides vital information regarding tumour microenvironment. Also different histologic types of tumours have been shown to have different perfusion parameters[21].

Considering all these, this study aimed at prospectively evaluating if perfusion CT could be an additional useful tool to multiphasic MDCT in the accurate characterisation of renal lesions, thereby aiding in further management.

Review of Literature

3. REVIEW OF LITERATURE

RENAL EMBRYOLOGY

The Urogenital system develops from a common mesodermal ridge (intermediate mesoderm) along the posterior wall of the abdominal cavity. It is formed in a cranial to caudal sequence divided into the pronephros, mesonephros and metanephros. The pronephros is rudimentary and non-functional. The mesonephros may function for a short time during the early fetal period. The metanephros forms the permanent kidney[22].

The Metanephros, which forms the permanent kidneys appears in the fifth week. Its excretory units develop from metanephric mesoderm. The development of the collecting duct system differs from that of the excretory units.

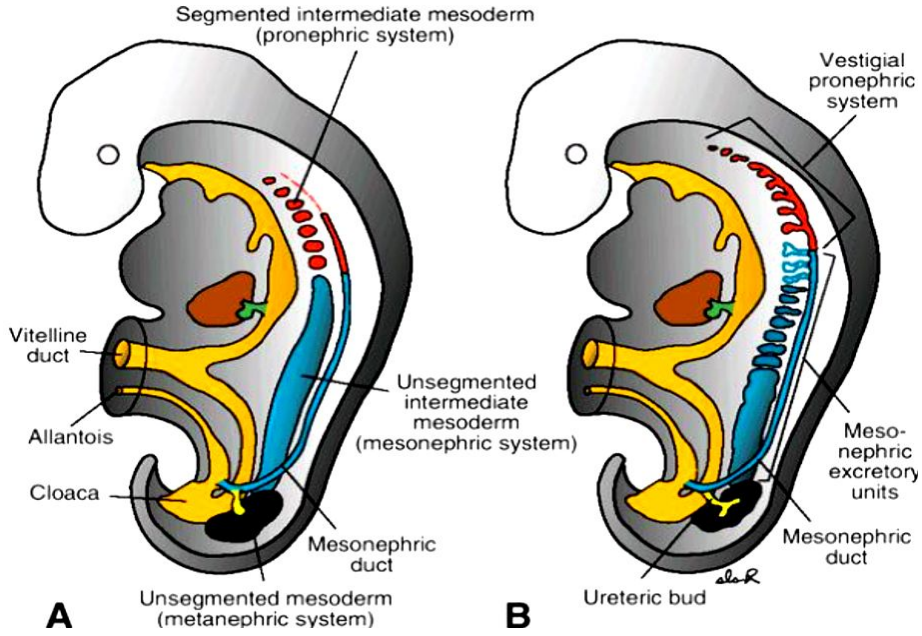


Fig 3.1 Division of the Intermediate mesoderm into pronephros, mesonephros, metanephros

Collecting System:

Collecting ducts of the permanent kidney develop from the ureteric bud, an outgrowth of the mesonephric duct. The bud penetrates the metanephric tissue, which is moulded over its distal end as a cap. Subsequently the bud dilates, forming the primitive renal pelvis, and splits into cranial and caudal portions, the future major calyces.

Each calyx forms two new buds which continue to subdivide until 12 or more generations of tubules have formed. The tubules of the second order enlarge and absorb those of the third and fourth generations, forming the minor calyces of the renal pelvis. During further development, collecting tubules of the fifth and successive generations elongate considerably and converge on the minor calyx, forming the renal pyramid.

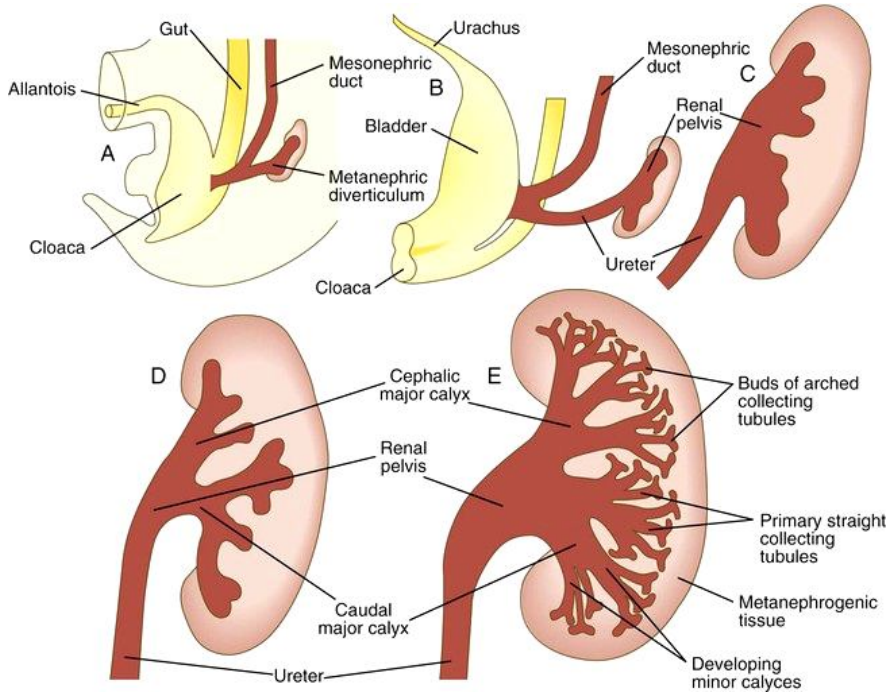


Fig 3.2 Development of the collecting system

Excretory System:

Each newly formed collecting tubule is covered at its distal end by a metanephric tissue cap. Under the inductive influence of the tubule, cells of the tissue cap form small vesicles, the renal vesicles, which in turn give rise to small S-shaped tubules. These tubules, together with their glomeruli, form nephrons, or excretory units. The proximal end of each nephron forms Bowman's capsule, which is deeply indented by a glomerulus. The distal end forms an open connection with one of the collecting tubules, establishing a passageway from Bowman's capsule to the collecting unit. Continuous lengthening of the excretory tubule results in formation of the proximal convoluted tubule, loop of Henle, and distal convoluted tubule.

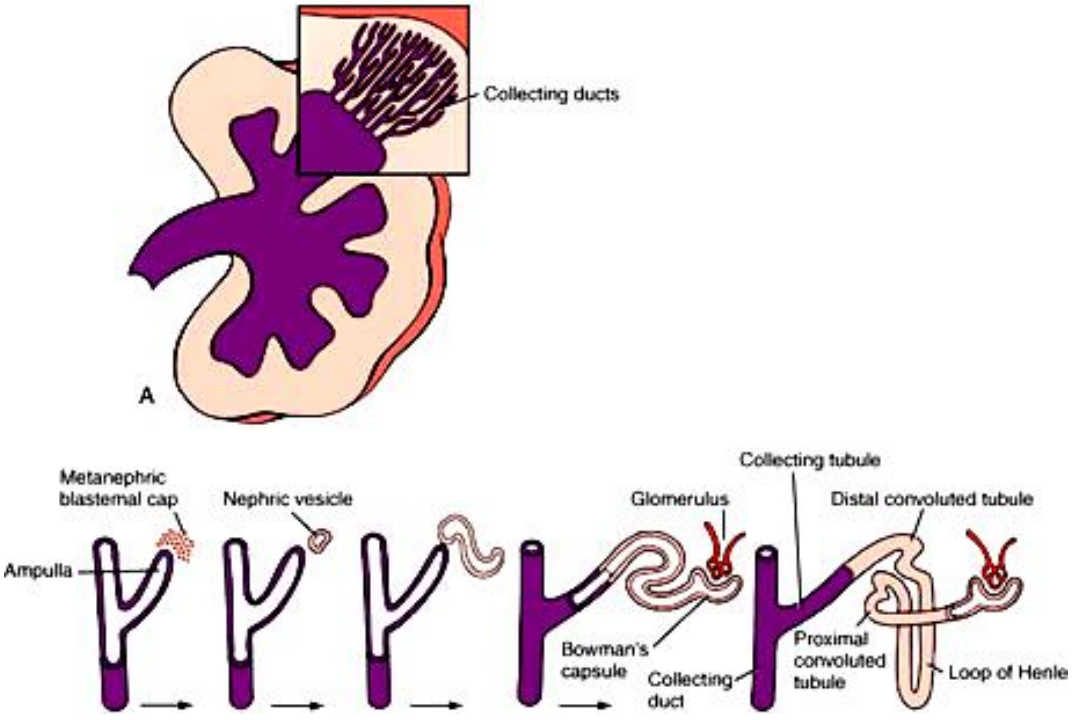


Fig 3.3 Development of the excretory unit

Position of the Kidneys:

The kidney, initially in the pelvic region, later shifts to a more cranial position in the abdomen.

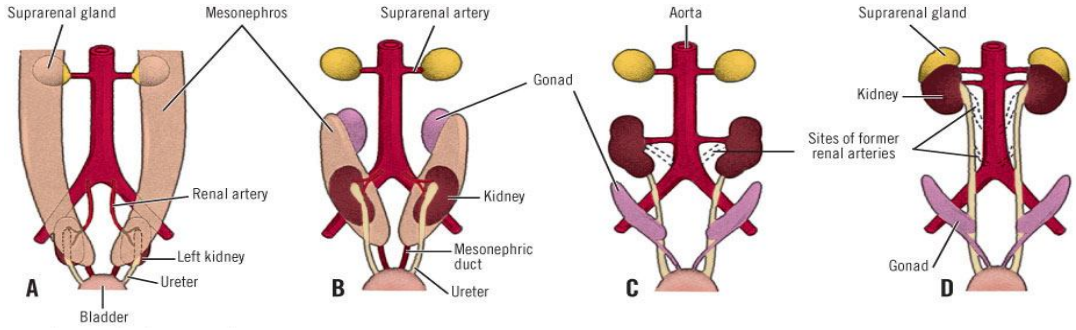


Fig. 3.4 Ascent of the kidneys

RENAL ANATOMY:

Kidneys are bean shaped retroperitoneal organs situated in the posterior abdominal region, situated in between T12 to L3 levels. Right kidney is at a lower level than left kidney because of its relationship with liver superiorly.

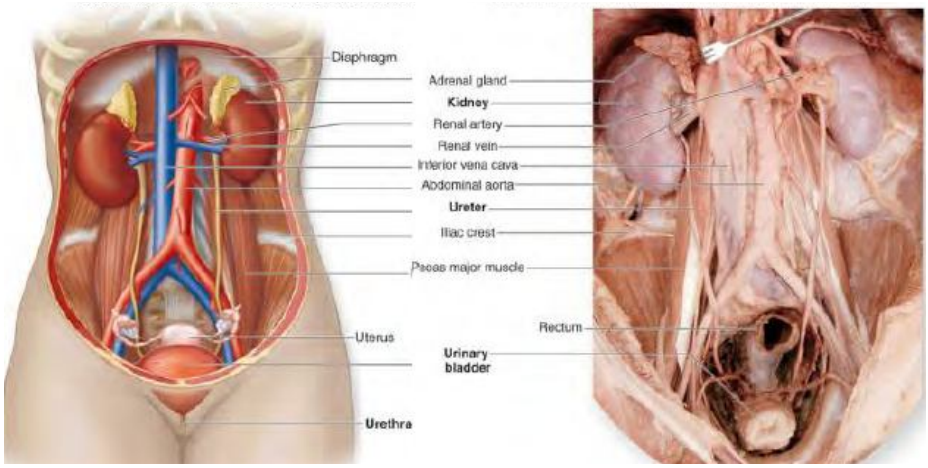


Fig 3.5 Normal position of the kidneys in the retroperitoneum

A. RENAL FAT and FASCIA

From innermost to outermost as follows:[23]

1. Renal capsule.
2. Perinephric/perirenal fat - Extraperitoneal fat which completely surrounds the kidneys.
3. Renal fascia - Membranous condensation of Extraperitoneal fascia. Divided into anterior and posterior layers which fuse laterally.
4. Paranephric fat - Accumulates posterior and posterolateral to kidneys.

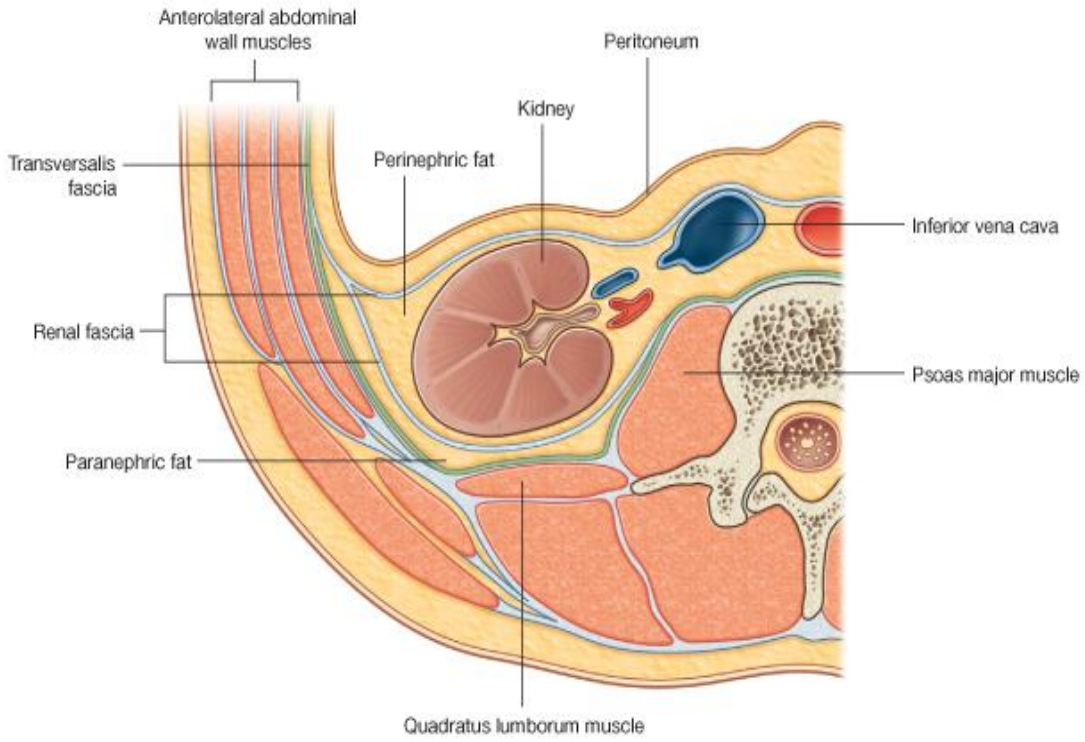


Fig 3.6 Organization of fat and fascia surrounding the kidney[23]

B. KIDNEY INTERNAL STRUCTURE

Hilum:

Renal hilum is seen on the medial margin of each kidney and constitutes the entrance and exit to renal vessels, lymphatics and nerves. Internally the renal hilum is continuous with the renal sinus. Perinephric fat continues into hilum and sinus and surrounds all structures.

Outer renal cortex:

It is a continuous band of pale tissue that completely surrounds the renal medulla.

Inner renal medulla:

Renal medulla is divided into multiple renal pyramids which are discontinuous aggregations of triangular-shaped tissue, separated by renal cortical columns.

- Bases of the renal pyramids (Corticomedullary Junction) are directed outwards, towards renal cortex.
- Apices (Renal papilla) are directed inwards, towards renal sinus. They contain Ducts of Bellini which empty urine into surrounding minor calyces via area cribosa.

Several minor calyces unite to form a major calyx. Several major calyces unite to form renal pelvis (continuous with ureter).

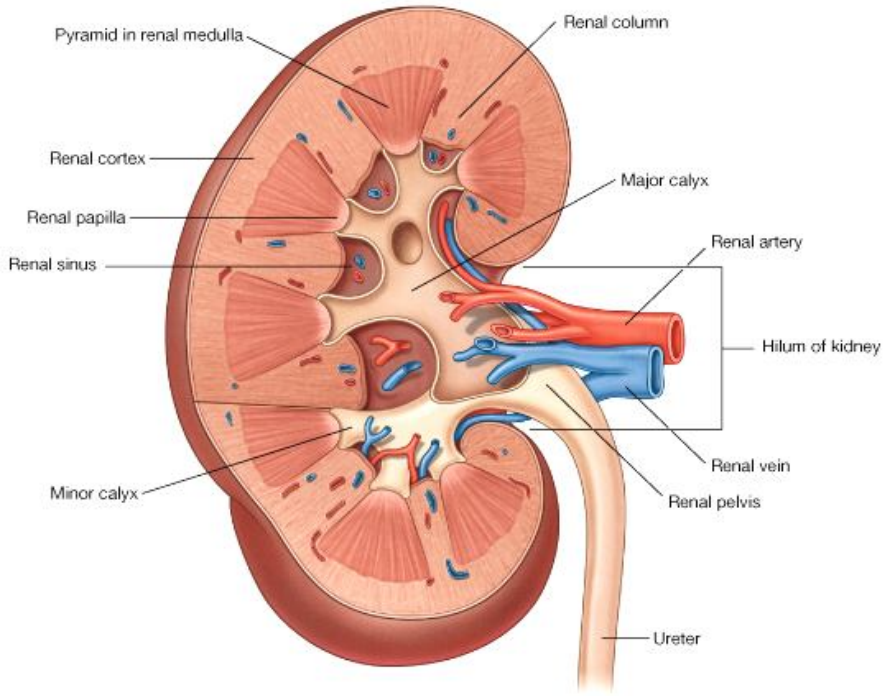


Fig 3.7 Internal structure of the kidney[23]

C. RENAL VASCULATURE

Renal arteries (lateral branches of abdominal aorta, usually arising at the level of L1-L2, inferior to origin of superior mesenteric artery) supply about 10% of the total blood volume to each kidney. Right renal artery is longer, passes posterior to IVC.

Renal artery divides into 5 separate Segmental arteries which supply different segments of kidneys. They do not anastomose with each other. This results in the distinct vascular segmentation of kidney, with each being surgically resectable.

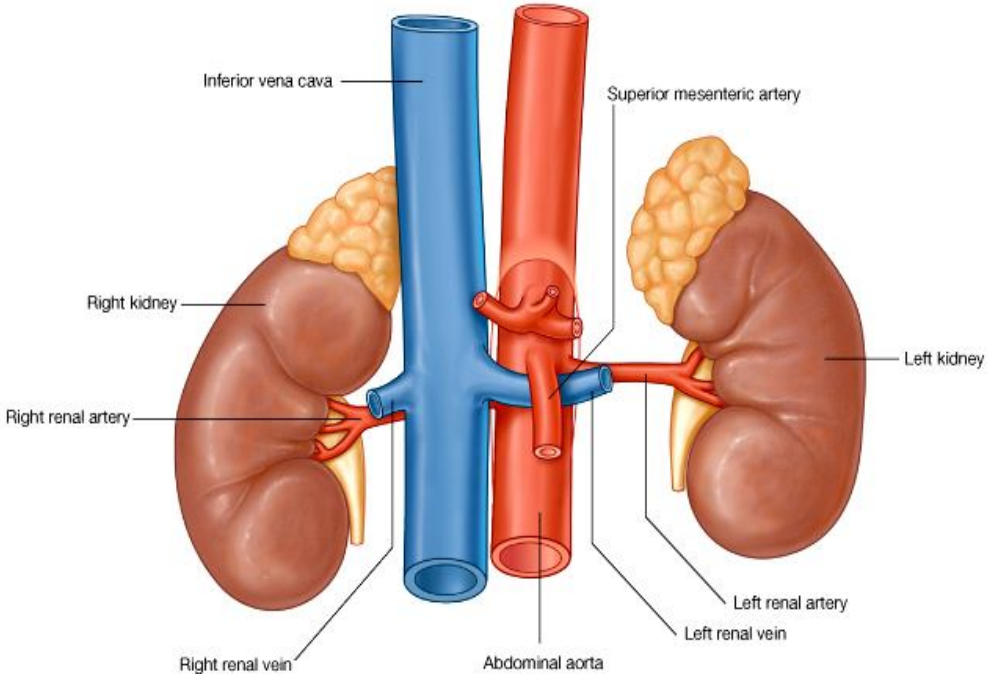


Fig 3.8 Renal Vasculature

Renal vasculature follows the following pathway.

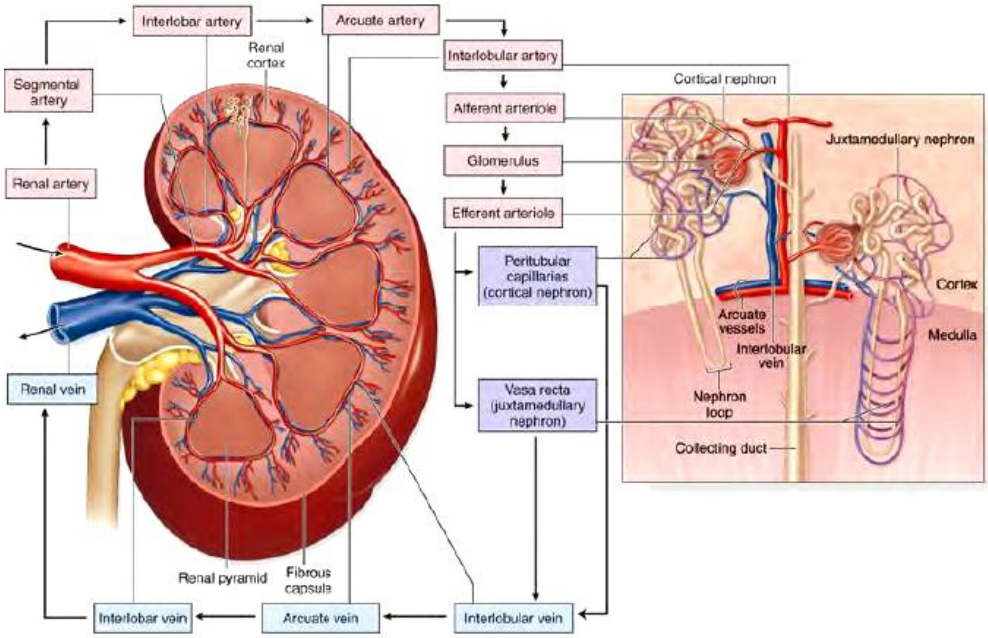


Fig 3.9 Renal vasculature and its pathway

CLASSIFICATION OF RENAL LESIONS:

1) **Benign tumours:**

- Renal cell neoplasms
    - Oncocytoma
    - Papillary adenoma
- Metanephric tumours
    - Metanephric adenoma
    - Metanephric stromal tumour
    - Metanephric adenofibroma
- Mesenchymal neoplasms
    - Angiomyolipoma
    - Leiomyoma
    - Hemangioma
    - Lymphangioma
    - Reninoma (Juxtaglomerular cell neoplasm)
    - Renomedullary interstitial cell tumour
    - Lipoma
    - Fibroma
- Mixed epithelial and mesenchymal neoplasms
    - Mixed epithelial & stromal tumours
    - Cystic nephroma

- Others
    - Rhabdomyoma
    - Neurofibroma

2) Malignant tumours:

- Renal Parenchymal tumours:
    1. **Adults** - Renal cell carcinoma (RCC)
        - Clear cell conventional RCC
        - Clear cell multilocular RCC
        - Papillary RCC
        - Chromophobe RCC
        - Collecting duct RCC .
        - Renal medullary carcinoma
        - Unclassified RCC
    2. **Children** - Wilms tumour (Nephroblastoma)
- Mesenchymal origin - Sarcoma
- Lymphoma
- Metastasis
- Tumours of collecting system:
    - Transitional cell carcinoma (TCC)
    - Squamous cell carcinoma of renal pelvis.

3) **Renal cystic lesions:**

- Serous renal cysts
- Complicated cysts (Benign / Malignant – Bosniak Classification System)
- Parapelvic and peripelvic cysts
- Adult polycystic disease
- Hydatid (echinococcal) cysts of the kidney

4) **Inflammatory masses:**

- Renal abscesses
- Acute focal pyelonephritis
- Malacoplakia

5) **Vascular masses:**

- Hematoma
- Aneurysms
- Arteriovenous malformations

WHO classification of tumours of the kidney

Renal cell tumours	
Clear cell renal cell carcinoma	8310/3
Multilocular cystic renal neoplasm of low malignant potential	8316/1*
Papillary renal cell carcinoma	8260/3
Hereditary leiomyomatosis and renal cell carcinoma–associated renal cell carcinoma	8311/3*
Chromophobe renal cell carcinoma	8317/3
Collecting duct carcinoma	8319/3
Renal medullary carcinoma	8510/3*
MiT family translocation renal cell carcinomas	8311/3*
Succinate dehydrogenase–deficient renal carcinoma	8311/3
Mucinous tubular and spindle cell carcinoma	8480/3*
Tubulocystic renal cell carcinoma	8316/3*
Acquired cystic disease–associated renal cell carcinoma	8316/3
Clear cell papillary renal cell carcinoma	8323/1
Renal cell carcinoma, unclassified	8312/3
Papillary adenoma	8260/0
Oncocytoma	8290/0
Metanephric tumours	
Metanephric adenoma	8325/0
Metanephric adenofibroma	9013/0
Metanephric stromal tumour	8935/1
Nephroblastic and cystic tumours occurring mainly in children	
Nephrogenic rests	
Nephroblastoma	8960/3
Cystic partially differentiated nephroblastoma	8959/1
Paediatric cystic nephroma	8959/0
Mesenchymal tumours	
Mesenchymal tumours occurring mainly in children	
Clear cell sarcoma	8964/3
Rhabdoid tumour	8963/3
Congenital mesoblastic nephroma	8960/1
Ossifying renal tumour of infancy	8967/0
Mesenchymal tumours occurring mainly in adults	
Leiomyosarcoma	8890/3
Angiosarcoma	9120/3
Rhabdomyosarcoma	8900/3
Osteosarcoma	9180/3
Synovial sarcoma	9040/3
Ewing sarcoma	9364/3
Angiomyolipoma	8860/0
Epithelioid angiomyolipoma	8860/1*
Leiomyoma	8890/0
Haemangioma	9120/0
Lymphangioma	9170/0
Haemangioblastoma	9161/1
Juxtaglomerular cell tumour	8361/0
Renomedullary interstitial cell tumour	8966/0
Schwannoma	9560/0
Solitary fibrous tumour	8815/1
Mixed epithelial and stromal tumour family	
Cystic nephroma	8959/0
Mixed epithelial and stromal tumour	8959/0
Neuroendocrine tumours	
Well-differentiated neuroendocrine tumour	8240/3
Large cell neuroendocrine carcinoma	8013/3
Small cell neuroendocrine carcinoma	8041/3
Phaeochromocytoma	8700/0
Miscellaneous tumours	
Renal haematopoietic neoplasms	
Germ cell tumours	
Metastatic tumours	

The morphology codes are from the International Classification of Diseases for Oncology (ICD-O) (917A). Behaviour is coded /0 for benign tumours; /1 for unspecified, borderline, or uncertain behaviour; /2 for carcinoma in situ and grade III intraepithelial neoplasia; and /3 for malignant tumours. The classification is modified from the previous WHO classification (756A), taking into account changes in our understanding of these lesions.

*New code approved by the IARC/WHO Committee for ICD-O.

Fig 3.12 WHO classification of tumours of the kidney[25]

RENAL CELL CARCINOMA:

Renal cell carcinoma (RCC) is the most common (accounting to 90 percent) of all the primary malignant renal neoplasms in adults[24].

RCC comprises of a heterogeneous, diverse group of neoplasms with different histology, biologic behavior, cytogenetic abnormalities, prognosis and response to treatment[26,27]. The clinical presentation includes hematuria, flank pain, and sometimes a palpable flank mass.

The median age of diagnosis is 65 years and most of the patients belong to the sixth to eighth decade of life[28,29]. Males are two to three times more affected than females[28,29]. Four percent is contributed by the hereditary RCCs and they have early-onset, multicentricity and bilaterality[30].

The 2004 WHO Classification of renal tumours in adults classifies RCC into various subtypes, of which clear cell type, papillary type and chromophobe type tumours contribute to 70%, 10%-15%, and 5%, respectively[31].

Other rare subtypes include carcinoma of the collecting ducts of Bellini, multilocular clear cell RCC, Xp11.2 translocation carcinoma, renal medullary carcinoma, carcinoma associated with neuroblastoma, mucinous tubular and spindle cell carcinoma and unclassified RCC[31].

Looking into the metastases from RCC, clear cell RCC account for 94%, papillary RCC 4% and chromophobe RCC 2% [26,27,32].

A) TYPES OF RCC:

1. CLEAR CELL RCC:

Clear cell RCC shows an acinar alveolar, or solid architectural pattern microscopically, and also has a clear or eosinophilic cytoplasm with a delicate vascular network[31]. Clear cell RCC shows exophytic growth with a heterogenous appearance. Moreover, **Pedrosa et al**[33] found that high grade lesions present with large size, intralesional necrosis, renal vein thrombosis, tumour capsule disruption and retroperitoneal vascular collaterals. The 5-year survival rate in clear cell tumours is 44%-69%[26,27].

2. PAPILLARY RCC:

Papillary type RCC comprises of malignant epithelial cells which form tubules and papillae on histology[31]. Papillary type are usually confined to the kidney and are generally of a smaller size (≤ 3 cm) and low grade and are homogeneous, well-circumscribed and peripherally located and hypovascular. Two pathologic subtypes of papillary RCC exist. Type 1 tumors have chromophilic cytoplasm and imaging shows more distinct margins and homogeneous density. Type 2 tumours have eosinophilic cytoplasm and show worse prognosis than type 1 tumours as they tend to be of a higher grade and stage[31]. The 5-year survival rate in papillary tumours is 82%-92%[26,27].

3. CHROMOPHOBE RCC:

Chromophobe RCC histologically shows large polygonal cells with prominent cell membranes and a reticulated cytoplasm with thick walled, eccentrically hyalinised blood vessels[31]. Chromophobe type RCC are well-circumscribed and homogeneous. Vascular involvement and perinephric infiltration are generally not seen. The 5-year survival rate in chromophobe tumours is 78%-92%[26,27].

B) MANAGEMENT AND FOLLOW UP:

The mainstay of treatment is surgery in localized RCC, for any subtype. Total nephrectomy is usually done, but in recent times "nephron-sparing" or partial nephrectomy has showed equally effective results in selective groups with local recurrence rates of < 2%[34] and 5-year survival rates of 87–90% [35]. Partial nephrectomy is indicated when tumour size is less than 4 cm, peripherally located lesions, renal insufficiency, bilateral renal tumours, and contralateral absent kidney.

In advanced cases, a tailored way of approach is recommended for management by systemic therapy which includes immunotherapy agents like interferon-α, targeted molecular agents like sunitinib, sorafenib, temsirolimus, and bevacizumab. Also the RCC subtype may influence the effectiveness of specific regime used in systemic therapy[36-38].

ANGIOMYOLIPOMA:

Angiomyolipoma (AML) is a benign renal tumour which is made up of smooth muscle, adipose tissue and dysmorphic blood vessels[39]. Mostly sporadic but may also be associated with tuberous sclerosis (<20%), or lymphangioleiomyomatosis[40]. AMLs commonly occur in middle age and have a female predilection. The diagnosis on imaging is by the detection of macroscopic fat. But, 5% of AMLs (lipid-poor AMLs) do not have sufficient amount of fat to be perceived by imaging[41] and these constitute a pitfall for misdiagnosis in imaging and leads to unnecessary surgery.

AMLs account for 18%-59% of the resected renal masses which have been ultimately classified as benign by histopathologic diagnosis[42,43]. Similar to clear cell renal carcinoma, AML with minimal fat also exhibit abnormal similar enhancement pattern during the early phase that is easily misdiagnosed as renal cancer. Unfortunately, studies have shown that imaging appearances of lipid poor AML and RCC, especially clear cell RCC may overlap[41-43] and there is no single pathognomonic radiologic finding to differentiate them.

RENAL ONCOCYTOMA:

Oncocytoma is a common benign renal tumour which accounts for 3%-7% of renal neoplasms[44,45]. The incidence peaks in the seventh decade, with a male predominance. Oncocytomas were found to be unilateral in 95%, bilateral in 5%, multiple in 6% and in 10%, a co-existing RCC was found[46].

Oncocytomas share some common imaging and histological findings with chromophobe RCCs[47,48]. Imaging findings which are suggestive of oncocytoma, such as homogeneous consistency, a well-defined margin, spoke-wheel enhancement, central stellate scar and segmental enhancement inversion may also be seen in cases of chromophobe RCCs[49-51]. Despite several studies showing promising results, discriminating an oncocytoma from RCC may be difficult at times, especially in small tumours.

RENAL LYMPHOMA:

Renal lymphoma can be primary or secondary. Primary lymphoma is rare and accounts for < 1% of extranodal lymphomas[52]**. El-Sharkawy et al**[53] found that renal lymphoma has five morphologic patterns on CT: "Enlarged lobular non-enhancing kidneys, focal single non-enhancing renal mass, bilateral multiple renal masses, bilateral diffuse areas of non-enhancing hypodensities and perirenal infiltrations from retroperitoneal extension".

Renal lymphoma is generally hypovascular and hence differentiating from a hypovascular RCC like papillary type RCC becomes challenging[54]. Also, extensive para-aortic adenopathy may be seen in type 2 papillary RCC which inturn can mimic secondary renal lymphoma[54]. In such equivocal cases, renal biopsy may be required for definite diagnosis. So that surgery can be spared in such patients, as lymphoma generally responds well to chemotherapy.

RENAL CYSTIC LESIONS: Bosniak Classification System[55]

Bosniak category	Features
I	A simple benign cyst with a hairline thin wall that does not contain septa, calcification or solid components. It measures as water density and does not enhance with contrast material.
II	A benign cyst that might contain a few hairline thin septa. Fine calcification might be present in the wall or septa. Uniformly high-attenuation lesions of <3 cm that are sharply marginated and do not enhance.
IIF	These cysts might contain more hairline thin septa. Minimal enhancement of a hairline thin septum or wall can be seen and there might be minimal thickening of the septa or wall. The cyst might contain calcification that might be nodular and thick but there is no contrast enhancement. There are no enhancing soft-tissue elements. Totally intrarenal non-enhancing high-attenuation renal lesions of ≥3 cm are also included in this category. These lesions are generally well marginated.
III	These lesions are indeterminate cystic masses that have thickened irregular walls or septa in which enhancement can be seen.
IV	These lesions are clearly malignant cystic lesions that contain enhancing soft-tissue components.

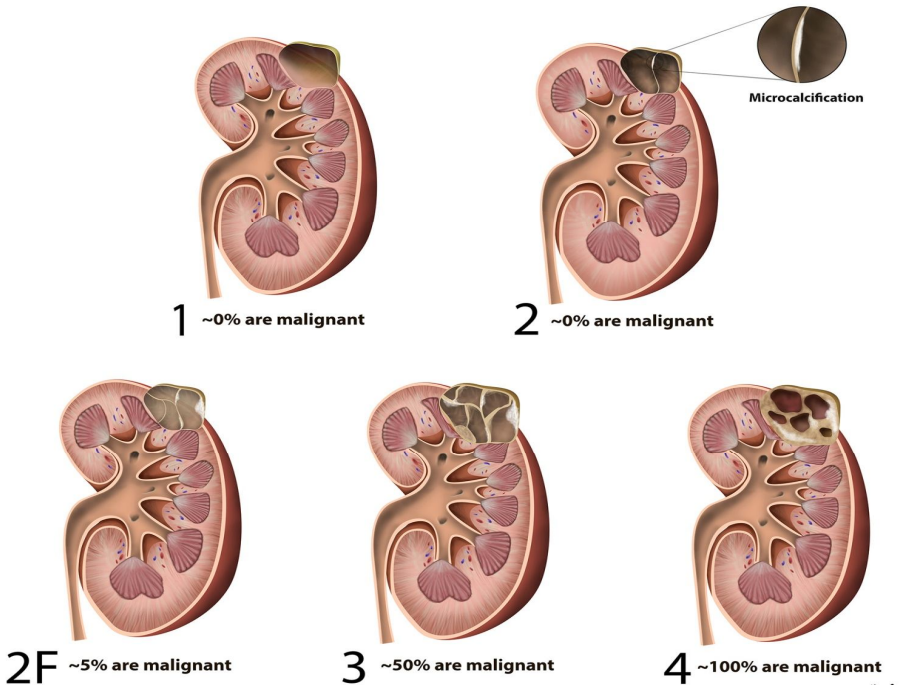


Fig 3.13 Bosniak Classification System of renal cystic lesions

IMAGING IN RENAL LESIONS

PLAIN XRAY AND IVP:

Calcifications are well identified, and large soft-tissue densities are noted in plain X-Rays. Calyceal compression, displacement, or amputation became recognized as evidence of renal tumours and intra- or extrarenal invasion in intravenous pyelogram. In the recent era, they have been replaced by other imaging modalities such as CT and MRI for the evaluation of renal masses.

ULTRASOUND (US):

Ultrasound is the initial imaging modality and is widely available, for detecting renal lesions and to narrow down the differential diagnosis, It is relatively safe, quick, cost-effective and provides real-time visualisation which is an added advantage compared to other modalities. Most of the renal lesions are being detected incidentally by ultrasound. When optimally performed, it helps in discriminating cystic from solid renal masses and also provides information on the internal structure of cystic masses, for example – septations, better than CT sometimes[56]. B-mode, M-mode, Doppler, ultrasound elastography along with computer-assisted three and four-dimensional imaging with US contrast agent, have shown increased diagnostic sensitivity and specificity in the detection and characterization of renal lesions.

Fig 3.14 Ultrasound image showing Angiomyolipoma which is seen as a well defined echogenic lesion in the lower pole of left kidney.

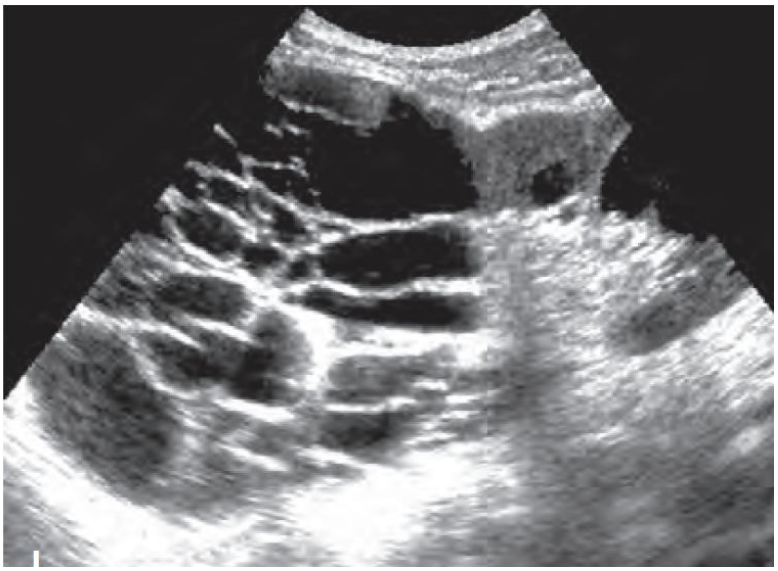


Fig 3.15 Ultrasound image showing a well defined partly exophytic, cystic mass with internal septations arising from the upper pole of left kidney.

COMPUTED TOMOGRAPHY (CT):

CT is the first choice for evaluating and staging a renal mass[57,58]. The corticomedullary phase (25-40 sec post injection) helps to differentiate between tumour and pseudotumour and to assess the degree of enhancement of the lesion. Strong enhancement is seen in clear cell carcinoma, lipid-poor AML and oncocytoma. However a tumour in the renal medulla can have the same attenuation as the surrounding renal parenchyma in this phase. Therefore, the nephrogenic phase of a tumour (80-100 sec post injection) is acquired which also provides information on tumour thrombus and possible vascular involvement. The optional excretory phase (around 8 minutes post injection) helps in the visualisation of the renal collecting system, ureters and bladder. It is not needed in the assessment of a renal cortical mass, but it should be done if transitional cell carcinoma is suspected.

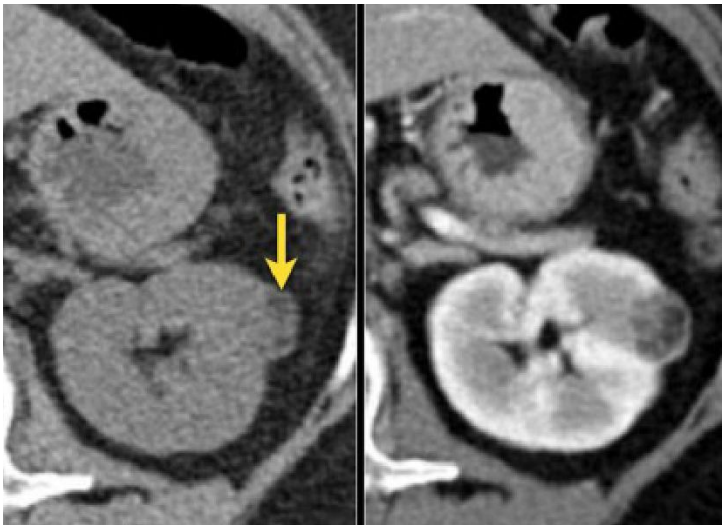


Fig 3.16 Contrast enhanced CT showing angiomyolipoma with areas of fat density seen arising from the left renal cortex.

Fig 3.17 Contrast enhanced CT showing typical features of clear cell RCC –ball type lesion causing smooth contour bulge, with heterogeneous enhancement and areas of necrosis

MAGNETIC RESONANCE IMAGING (MRI):

MRI is better when compared to CT in the assessment of a cystic lesion as it depicts the enhancement better and also differentiates CT-pseudoenhancement from real enhancement. Hemorrhagic or proteinaceous cysts and angiomyolipomas with macroscopic extracellular fat show high signal on T1-weighted images. However intracellular fat does not produce a high signal on T1-weighted images but it shows a signal drop in the out of phase images. 82% of clear cell RCCs contain intracellular fat, which therefore accounts to 90% specificity for the diagnosis of clear cell renal cell carcinoma. Low T2-signal favors papillary RCC or can be seen in minimal fat angiomyolipoma. High T2 is typically found in clear cell RCC but is non-specific, since it can also occur in oncocytomas. There is much overlap seen between malignant and benign tumours.

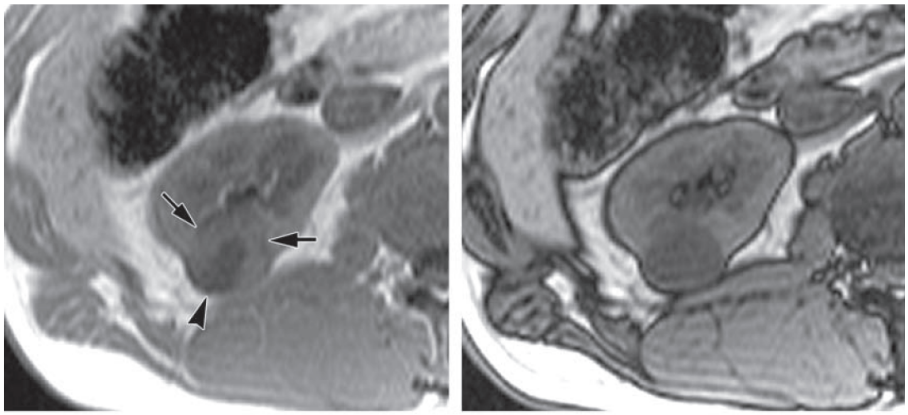


Fig 3.18 Clear cell RCC (a) Axial in-phase T1-weighted MR image shows a right renal mass with a thick isointense rim (arrows) and hypointense centre (arrowhead) (b) On an axial opposed-phase T1-weighted MR image, the mass appears homogeneous and is hypointense.

Diffusion MRI can be used to detect and characterize diffusion restricting lesions. **Wang et al.** retrospectively evaluated 85 renal masses imaged with DWI and assessed the ability of ADCs to predict RCC subtype [60].

Recently Perfusion MRI has been applied in the characterisation of renal masses, providing histologic information such as subtype and grading. **Lanzman et al.**[81] showed that oncocytomas demonstrated higher levels of perfusion than all types of RCC. **Sun et al.**[82] used DCE MRI and retrospectively examined pathology-proven clear cell, papillary, and chromophobe RCCs masses. They concluded that each subtype showed a characteristic signal intensity change and clear cell RCC can be distinguished from papillary RCC with 93% sensitivity and 96% specificity.

CONTEMPORARY TRENDS AND FUTURE INVESTIGATIONS

As seen already, renal masses are a heterogeneous group of tumours that are further subdivided into different histological entities having different survival rates and oncologic outcomes. And, around 30% of surgically resected renal masses less than 4 cm, show a benign pathology (e.g. oncocytoma, AML)[61,62]. Also a significant number of small renal masses are of the chromophobe or papillary RCC subtype and have a better disease specific survival compared to clear cell RCC. Therefore identifying the histology preoperatively has a definite advantage as both the less aggressive and benign tumours can be managed potentially with active surveillance, whereas surgical removal is needed in case of more aggressive tumours.

However, no single imaging modality has yet proven to be reliably capable in differentiating benign from malignant tumours or between the histologic subtypes of malignant tumours. Biopsy-based risk can be a potentially viable option to determine surgical excision versus active surveillance, but biopsy being an invasive procedure poses a risk of morbidity[63]. Ideally, preoperatively, a patient could undergo a non-invasive imaging study which helps to ascertain the renal mass histology. Newer imaging modalities like CT perfusion imaging and molecular imaging may bridge the gap between routine imaging (CT/MRI) and histologic diagnosis (biopsy).

PERFUSION CT IMAGING

Perfusion CT has shown tremendous progress since its invention and is slowly widening its applications from the research aspects to routine clinical care especially in the oncological setting.

Perfusion CT imaging can be readily incorporated into the existing CT protocols which provides the mainstay for anatomical imaging in the field of oncology, to provide information regarding tumour angiogenesis.

By capturing physiological information reflecting the tumour vasculature, perfusion CT can be a valuable tool for diagnosis, tissue characterization, risk-stratification and therapeutic monitoring.

BASICS OF CT PERFUSION

The basic principle of CT perfusion is based on the temporal changes in the tissue density following administration of iodinated contrast media intravenously.

The chronological change in the tissue density depends on the iodine concentration and reflects the nature of tissue vascularity. During the passage of contrast in the tissues, by rapid sequential acquisition of images perfusion CT allows in the quantification of tissue vascularity.

Dynamic contrast enhanced imaging is the most common method used for imaging studies of the microcirculation in the tissues other than brain. The temporal kinetics of enhancement following contrast injection depends on

the local circulatory system, the mode of injection, injection dose, rate, type and concentration of the contrast agent. It can then be analyzed using various strategies to obtain visual criteria, semi-quantitative criteria or better, microvascular physiological parameters.

TECHNICAL PRINCIPLES IN ACQUISITION OF PERFUSION CT

A conventional CT perfusion protocol consists of two acquisitions:

1) Baseline acquisition (without contrast enhancement) - to select the appropriate area for study.
2) Dynamic acquisition of the selected volume over time – measurement of temporal changes in tissue density after contrast injection.

Time-density curve is acquired by subtracting the baseline values from each of the serial dynamic CT studies. A small volume (40–70 mL, depending on the concentration of contrast media) given at high flow rates (> 4 mL/s) followed by saline flush of 20–40 mL given at a similar flow rate is needed , thereby obtaining a narrow bolus for optimal perfusion analysis.

The dynamic image acquisition is divided into two different phases. In the early phase, high temporal sampling is required for image acquisition (less than 2 seconds). This first-pass phase lasts up to 45 seconds

usually, from the starting time of administration of contrast agent. Enhancement is attributable mainly to the contrast within the intravascular space.

In the second phase (interstitial phase), contrast material passes into the extravascular extracellular compartment, which is influenced by vascular permeability. A lower temporal sampling of 5–15 seconds per acquisition is required in this second phase. The sampling interval and total time within the interstitial phase are dependent on the type of analysis model used.

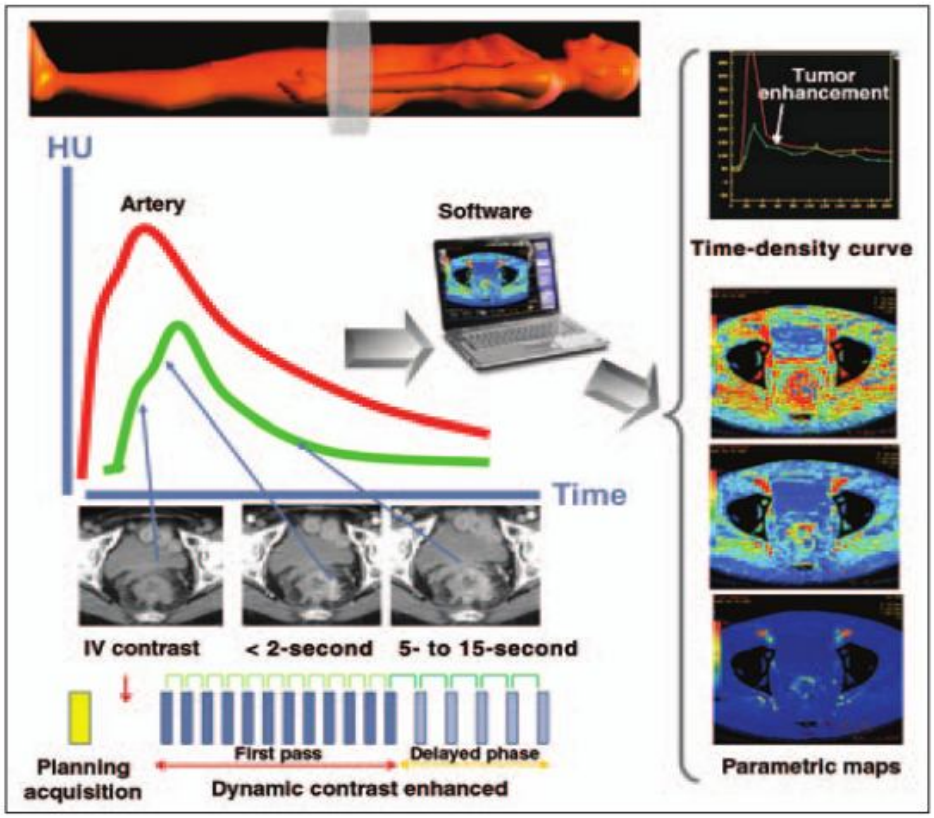


Fig 3.19 Technical principles of perfusion CT[65]

MECHANISMS INVOLVED IN TISSUE ENHANCEMENT KINETICS

Following the injection of contrast media through intravenous route, the contrast gets distributed within the tissues which results in increasing tissue density in CT. Two essential phenomena occur simultaneously[64]:

1) Perfusion in the microcirculatory network - Pure tissue perfusion.
2) Accumulation in the interstitium, followed by release due to capillary leakage.

These two phenomena seem to have differing time courses and kinetics, but overlap occurs, leading to a considerable source of confusion.

The tissue enhancement which occurs following contrast administration may be divided into two phases[8].

In the initial phase, the enhancement is mainly because of the contrast within the intravascular space and therefore it is determined by the blood flow and the blood volume.

Later the second phase occurs as the contrast material passes from the intravascular to the extra vascular compartment across the capillary basement membrane, where the enhancement results from the distribution of contrast in both the intravascular and the extravascular compartments. This depends on the permeability of capillaries to the contrast agent.

The contrast agent present in the volume of interest reflects the summed amount of contrast agent within the blood vessels and the contrast agent that has moved to the interstitial space by passive diffusion

Another requirement for perfusion CT analysis is the selection of a vessel (usually an artery) supplying the tissue of interest to obtain a time-intensity curve (the arterial input function) by placing a region of interest (ROI) into the lumen of the vessel.

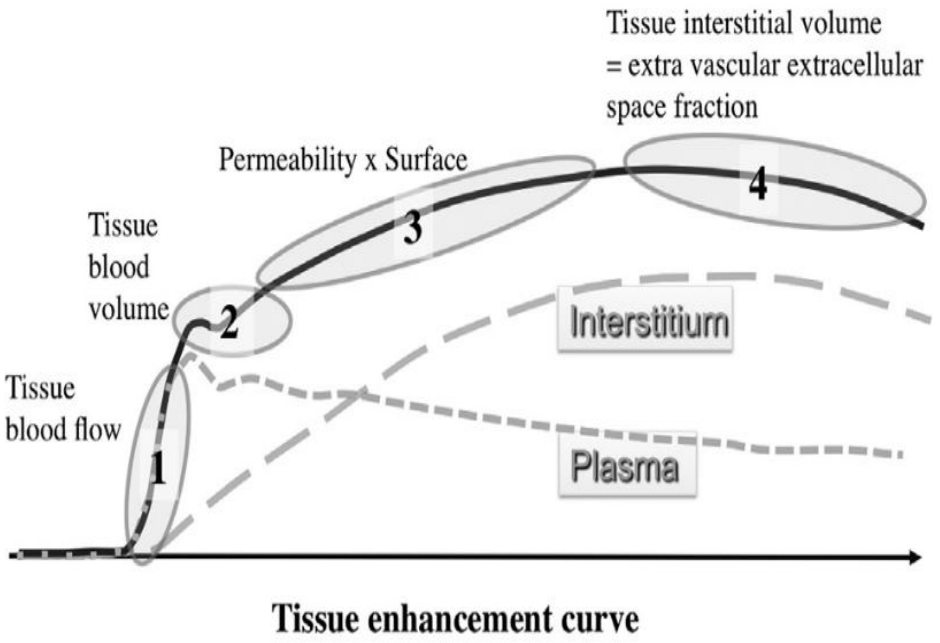


Fig 3.20 Tissue enhancement curve: sum of the plasma component (small dots) and the interstitial component (large dots)[64].

MATHEMATICAL MODELING TECHNIQUES

The dynamic CT data obtained is used to measure two functional CT paradigms: i.e. perfusion measurements and the permeability studies[8].

The two most commonly used mathematical modeling techniques for quantifying different perfusion parameters from the CT data acquired from the tissue and the vascular system are: Compartmental analysis and De-convolution analysis[67,68].

Both the methods require obtaining the time attenuation data, from the arterial input, for estimating the tissue vascularity and to correct the inter patient variations in the bolus geometry[67,68].

1. COMPARTMENTAL ANALYSIS:

This analytic technique is based on a single compartmental or a two compartmental model[67,68].

The single compartmental model estimates the tissue perfusion and it considers both intravascular as well as extra-vascular spaces as a single compartment. This model is based on the Fick's principle and tissue perfusion is calculated based on the conservation of mass within the system[67,68]. It estimates the tissue perfusion either from the peak height or the maximal slope of the same tissue concentration curve, which has been normalized to the arterial input function[68,9].

The two compartmental model is used for evaluating the capillary permeability and also the blood volume[68,9]. This assumes the intravascular and the extra vascular spaces as two separate compartments and it measures the perfusion parameters using Patlak analysis technique. It is a nuclear medicine processing technique which is used in determining the rate constant of tissue uptake of a tracer from the vascular space by using the tracer concentration values in tissue and blood. Simply to say, it quantifies the passage of contrast from the intravascular space into the extra vascular space[8].

2. DECONVOLUTION ANALYSIS:

This method is based on the use of the arterial as well as the tissue time-concentration curves in order to calculate the impulse residue function for the tissue.

Impulse residue function(IRF) is a theoretical tissue curve which is obtained from the direct arterial input with the assumption that the concentration of contrast in the tissue is linearly dependent upon the input arterial concentration when the blood flow remains constant[67,68].

After flow correction is made, the height of this curve determines the tissue perfusion and the area under the curve decides the relative blood volume[68]. For estimating the capillary permeability, a distributed parameter model which consists of an extended de-convolution model, is used.

Table showing comparison of analytic models[65]

Model	Compartment	Measure	Assumptions	Acquisition	Advantages and Disadvantages
Fick; uses maximal slope or peak height of tissue concentration curve normalized to arterial input function	Single	BF	No venous outflow	45 s (length), < 2 s interval	Less sensitive to movement
Patlak; quantifies passage of contrast material from intravascular into extravascular space	Dual	EF, BV	Well-mixed compartments; one-way transfer only	< 2 min (length), < 5 s interval	Better for organs having complex microcirculation (kidney, spleen)
Johnson Wilson distributed parameter; based on use of arterial and tissue-time concentration curves to calculate impulse residue function for tissue	Dual	BF, BV, EF	Constrained impulse residue function	< 2.5 min (length), < 2 s interval in first pass, < 15 s interval in delayed phase	Less sensitive to noise, uses lower tube current, higher temporal resolution

BF-Blood Flow, BV-Blood Volume, EF-Extraction Fraction

COMPARTMENTAL vs DECONVOLUTION ANALYSIS:

They both differ in terms of their theoretical assumptions, and their susceptibility to noise and motion[68].

Compartmental analysis is based on the assumption that the bolus of contrast agent is retained within the organ of interest during the time of measurement. This may result in underestimating the perfusion values in organs which have rapid vascular transit or in cases of large bolus injection[68].

Whereas, deconvolution model assumes IRF shape to be a plateau with a single exponential wash-out. Though for most of the organs this assumption works out well, it might not be suitable for the organs like kidney and spleen which have complex microcirculations[68].

Hence, compartmental analysis is preferably used for organs with complex circulatory pathways.

CALCULATION OF CT PERFUSION PARAMETERS

After acquisition of CT data, the CT perfusion parameters are calculated by using either a model-based or a model-free approach. Regardless of what algorithm is used, multiple image processing steps are to be performed for calculating the CT perfusion parameters.

The imaging processing steps include motion correction or image alignment, arterial input function selection, defining the region of interest (ROI), and voxel wise computation of the various perfusion parameters.

Color-coded perfusion maps of Blood volume(BV), Blood flow(BF), Permeability(PMB) and Mean transit time(MTT) are then generated using automated software at the workstation.

PERFUSION PARAMETERS

Perfusion CT facilitates the analysis of renal function through the measurement of various perfusion parameters like

1) Blood Volume (BV),

2) Blood Flow (BF),

3) Permeability surface area product (PMB or PS),

4) Mean Transit Time (MTT)

Blood volume (BV)

Blood volme corresponds to the volume of capillary blood contained in a certain volume of tissue (expressed in mL blood/100 mL of tissue).[64]

Blood flow (BF)

Blood flow corresponds to the blood flow entering (and exiting) the vasculature of a volume of tissue in a given period (expressed in mL of blood/min/100 mL tissue).[64]

Permeability surface area product (PMB)

Permeability surface area product is the flow of molecules through the capillary membranes in a certain volume of tissue[64]. It is the product of permeability and the total surface area of capillary endothelium in a unit mass of tissue or tumour (expressed in mL/min/100 mL tissue).

Mean Transit Time (MTT)

Mean Transit time is the mean time taken by the blood to traverse through the capillary network - time between the arterial inflow and the venous outflow (expressed in second)[64].

Table showing interpretation of CT perfusion parameters [65]

BV/BF (Often Coupled)	PS	Interpretation
↑	↑	New vessel formation (angiogenesis) with varying degrees of maturation
↑	↔ or ↓	Mature vasculature with intact basement membrane (e.g., intact BBB)
↓	↓	Necrosis
↓	↔ or ↑	Inflammation or granulation tissue or early fibrosis
↔ or ↓	↑↑	Poor compartmentalization of contrast agent; largely immature vessels

BF-Blood Flow, BV-Blood Volume, PS – Permeability surface area product

MICROVASCULAR DENSITY(MVD)

Microvascular density (MVD) is a pathological marker which is a measure of neoangiogenesis and it predicts the aggressiveness and prognosis of various neoplasms. Intratumoral MVD is also a direct measure of vascular window via which tumour cells pass to spread to distant sites.

To calculate MVD, initially the area containing the maximum number of microvessels (the "hotspot" area) is identified and then individual microvessels are counted. The number of vessels in multiple areas within the tumour are counted and averaged as MVD.

Tumoral MVD, however, does not distinguish new blood vessels from the native ones, does not mark actively proliferating endothelial cells, and does not correlate with the degree of endothelial cell proliferation.

An excellent surrogate marker of this microvascular density is tumour Blood Volume (BV) and it thus helps to predict the grade and prognosis of the tumour.

TECHNICAL LIMITATIONS AND DRAWBACKS OF PERFUSION CT

Acquisition effects like streak artifact from high concentration of contrast, motion artifacts from bowel peristalsis or breathing), technical reproducibility and variability caused by different protocols and observers will influence the values of CT perfusion parameters.

Tumour vascularity measurements obtained using different analysis methods and commercial software packages made available by different vendors are not directly interchangeable, and show up to 46% difference between the values, and thus have to be corrected appropriately in case inter-platform or inter-model comparisons are to be made[70,71].

The choice of regions of interest (ROIs) which is the key area of perfusion analysis must be selected adequately to avoid sampling errors. In the arterial input function, the artery which is used to generate the arterial time-density curve should be large enough to avoid averaging with the surrounding tissues signal which will lead to BF overestimation. The parameter values can differ depending on the size of the tumour ROI, whether the whole tumour is included, or whether areas of necrosis are excluded. And it has been shown that calculating the parameters on a limited section may entail greater measurement variability and such values may not be representative when tumours tend to be large and heterogeneous[72,73].

Another major drawback to be considered is the radiation dose of CT perfusion.

PREVIOUS STUDIES ON PERFUSION CT IN RENAL LESIONS:

A review of the literature revealed several publications using CT perfusion in renal masses, in which various tumours and their subtypes were investigated and the perfusion parameters were compared.

Chen, Chao, et al.[7] demonstrated that BV was found to be significantly different between AML with minimal fat and RCC. Among the subtypes of RCC, clear cell RCC showed significantly higher BF and BV than papillary RCC and higher BV than chromophobe RCC.

Chen Y et al.[20] showed that there was a significant difference between BF, BV, MTT, and PS of normal renal cortex (454.32±110.90 mL/min/100g, 23.53 ± 5.71 mL/100g, 3.62 ± 1.38s, 63.95 ± 18.85 mL/min/100 g) and RCC (261.96 ± 175.86 mL/min/100 g, 17.17 ± 8.34 mL/100 g, 7.08 ± 3.42 s, 25.07 ± 13.20 mL/min/100 g).

Chen Y et al.[20] also demonstrated that BF and BV among RCC histologic subtypes were significantly different, whereas MTT and PS were not. MVD of RCC positively correlated with BF, BV, and PS, but not with MTT and thus may reflect the angiogenesis of RCC.

Sun Hao et al.[74], in his study, showed significant differences in perfusion parameters between the renal mass parenchyma and the normal renal cortex, and also significant differences were seen between any two pathological types of renal masses except for renal pelvic Transitional cell carcinoma(RPTCC) and angiomyolipoma(AML).

Gigli et al.[21] demonstrated a correlation between tumour histological subtype and perfusion index. Clear cell RCC of different Fuhrman grades showed statistically significant differences in perfusion values, with high perfusion indices associated with high microvessel density.

Zhang YL et al.[75] reported that PF(Perfusion Fraction) and BV(Blood volume) values are significantly higher in high-grade CCRCC than in low-grade CCRCC.

Reiner, Caecilia S., et al.[77] reported that BF and BV of RCC, showed significant correlations with the microvessel density. Also it was shown that Blood flow (BF), Blood volume (BV), and K^{Trans} were significantly higher in RCCs with less than 50% necrosis than in those with 50% or greater necrosis.

In the study by **Mazzei FG et al.**[76] it was found that PS and MTT values were significantly lower in malignant lesions than in the normal cortex and PS, MTT, and BF values were also statistically different between oncocytomas and malignant lesions.

Ng, Chaan S., et al.[78] reported that a significant increase in the tumour blood flow and a significant decrease in the tumour MTT was seen in metastatic RCC.

Chen, Chao et al.[79] demonstrated that tumour size and PS were significantly independent indexes for differentiating high-grade from low-grade clear cell RCC.

Fournier, Laure S., et al.[80] showed that, among the patients receiving antiangiogenic drugs, the baseline perfusion parameters were higher in responders compared to the stable patients and also there was a significant decrease in BF and BV in those patients after the first cycle of treatment.

Aim of the study

4. AIM OF THE STUDY

PRIMARY OBJECTIVES

1) To acquire CT perfusion parameters (BF - Blood Flow, BV - Blood Volume, PMB - Permeability) within the renal lesion and in the normal renal parenchyma.

2) To study the differences among the CT perfusion parameters obtained from various renal lesions and to correlate with the histopathological diagnosis, and grading.

3) To find out the sensitivity and specificity of the CT perfusion parameters that can be used to differentiate malignant tumours like renal cell carcinoma from other benign tumours of the kidney.

SECONDARY OBJECTIVES

To analyse the correlation between the CT perfusion parameters values of normal renal parenchyma with that of various benign and malignant renal lesions.

Materials and Methods

5. MATERIALS AND METHODS:

5.1 Study Area	:	Barnard Institute of Radiology, Madras Medical College, Chennai.
5.2 Study Period	:	6 months (January 2017 – June 2017)
5.3 Sample Size	:	40
5.4 Study Design	:	Prospective study

5.5 Inclusion Criteria:

- Age between 20 and 80 years, both sexes.
- The presence of solitary renal lesion diagnosed by USG / Conventional CT, with suspected Renal cell carcinoma scheduled for resection.

5.6 Exclusion Criteria:

- Lactating and pregnant females whatever the gestational age.
- Patients with impaired renal function (serum creatinine level higher than 1.3 mg/100 ml).
- Presence of more than one renal lesion.
- Patients with metastasis.
- Patients with simple renal cysts (Bosniak 1 & 2).
- Patients with history of allergy to contrast material.
- Uncooperative patients / patients with breathing difficulties.

5.7 METHODOLOGY:

This prospective study was performed after obtaining clearance from our Institutional Ethics Committee and institutional informed consent guidelines were observed.

5.7.1 Study Population:

Patients referred from Urology department with renal lesion diagnosed on US / Conventional CT, who are willing for CT perfusion were included in this study during the period from January 2017 to June 2017.

The patients were screened using the drawn inclusion/ exclusion criteria. Relevant entries in the proforma for each patient were made after reviewing his/her case sheet & previous medical records.

The final population enrolled in this study composed of 40 patients diagnosed as having renal lesion by ultrasound / Conventional CT, with suspected renal cell carcinoma, scheduled for surgery.

All patients were required to provide written informed consent before study participation.

5.7.2 CT Examination:

All CT perfusion studies were done using 16 SLICE CT scanner (SOMATOM EMOTION , SIEMENS HEALTHINEERS).

The imaging parameters were 110 kVp tube voltage, 120 mAs tube current, 0.5 s gantry revolution time, 512 X 512 pixel (spatial resolution), and 1.2 mm reconstructed slice thickness.

Scanning was performed as follows:

First, an unenhanced single image was obtained to ensure that the kidneys would be completely covered by the imaging field. Predefined scan volume for the tumour (predominantly trying to include the solid areas) was determined in the *z*-axis to cover the lesion for the CTp study.

Secondly, a bolus of 50 ml of low osmolar non-ionic contrast material Iohexol 350 (Omnipaque 350) was injected through a 18-gauge cannula placed in the volar aspect in the cubital vein at a flow rate of 5 ml/s using a power injector.

Following which dynamic volume CT scanning was initiated after the delay time, which was 6 seconds after the beginning of the contrast agent injection in order to ensure the acquisition of a little non enhanced baseline data both to allow the software to plot the enhancement change over time.

The dynamic cine acquisition consisted of 4 contiguous sections, collimated to 5 mm, by using a cine-mode acquisition without table movement. Total duration time was approximately 60 seconds with appropriate temporal resolution in order to include both first-pass enhancement and delayed phase.

5.7.3 Image Post Processing and Analysis:

Image analysis and post processing was done using syngo® Body Perfusion CT (Body PCT) software. For the CTp analysis, a processing threshold (CT value range) between -30 and 150 Hounsfield units (HU) was utilised to optimise visualisation of the soft tissue. On transverse CT images, the slice showing the maximal transverse tumour diameter was chosen for analysis.

After motion correction and automatic segmentation, a circular ROI was placed in the proximal abdominal aorta is to obtain the arterial input function. An arterial time-density curve for the entire acquisition time of the study was generated automatically.

Time-attenuation curves were obtained and quantitative perfusion parameters were calculated by applying body perfusion software using Patlak analysis. Four types of parameter maps were generated for each patient . They are,

- Temporal maximum intensity projection (MIP) in Hounsfield units (HU),
- Blood Volume - BV (ml/1000 ml),
- Blood Flow - BF (ml/100 ml/min) and ,
- Permeability - PMB (0.5ml/100 ml/min)

Initially, ROIs were drawn manually (maximum 1 cm^2) on the MIP images, on the solid part of the renal tumour, excluding areas of necrosis, calcifications, vessels, or cystic / hemorrhagic areas. The ROIs were then automatically copied onto the perfusion maps and corresponding BV, BF and PMB values were acquired.

For every patient, reference ROIs were also drawn on the healthy normal renal cortex of the same kidney and contralateral kidney and the mean perfusion parameters were obtained as control values.

5.7.4 Histopathology:

All the patients were followed up and histopathological reports were collected from the pathology department.

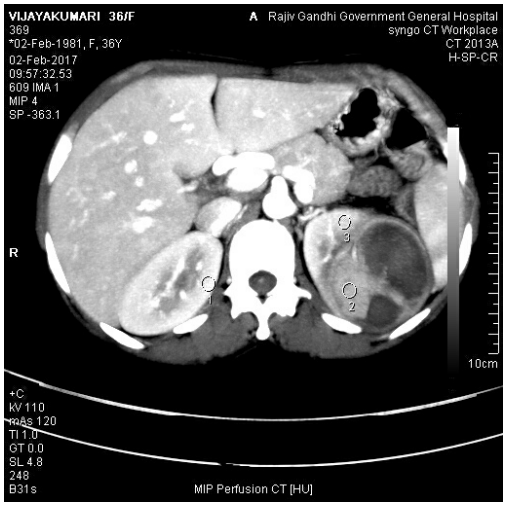
The surgical specimen consisted of radical nephrectomy in 34 out of 40 (85%) patients and partial nephrectomy in 6 out of 40 (15%) patients. The pathologist and radiologist jointly took care to ensure sampling at a tumour level corresponding to the level at which CTp was performed.

All the tumours were staged based on the last TNM classification system and were subjected to histopathological analysis, typing and subtyping. The Fuhrman grading system (I-IV) was used to grade the clear cell RCC. Grades I and II were considered low-grade clear cell carcinoma, grades III and IV were considered high-grade clear cell carcinoma.

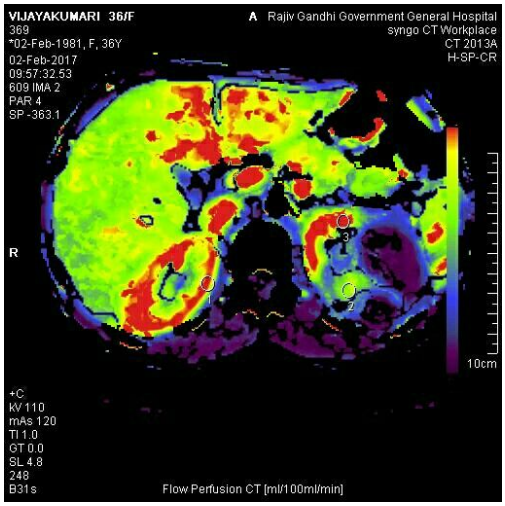
Representative Cases

CASE 1

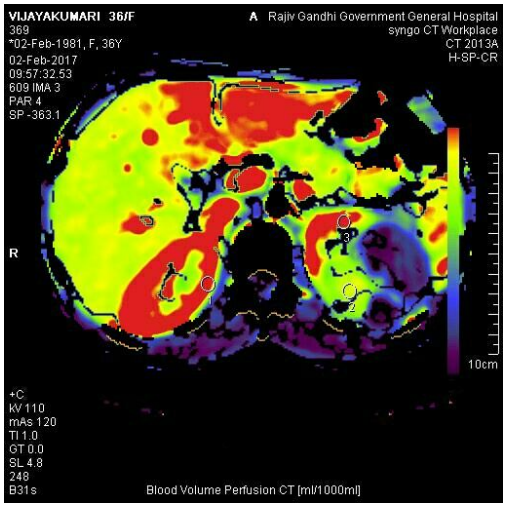
History: 36 years old female patient presented with a partially exophytic left renal mass with both cystic and solid components, and thick septations.



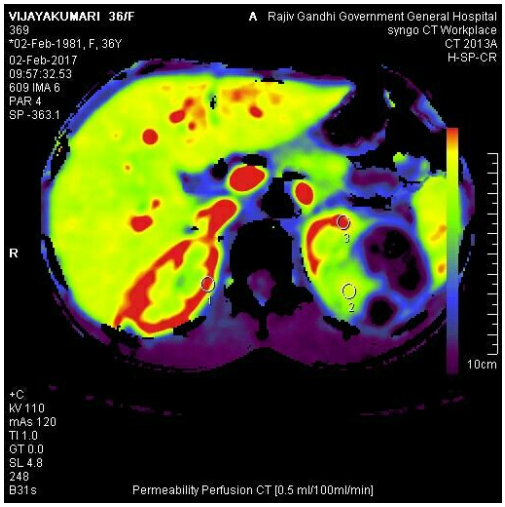
MIP PERFUSION CT (HU)



BLOOD FLOW (BF)



BLOOD VOLUME (BV)



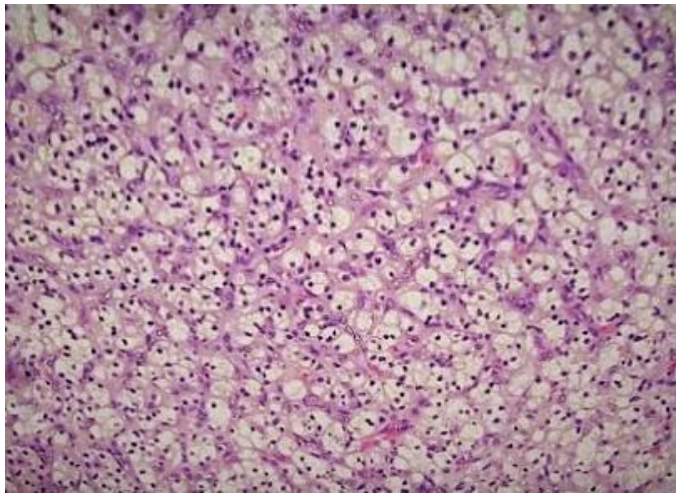
PERMEABILITY (PMB)

CT Perfusion Interpretation:

Parameters	Unit	Within the lesion (Mean values)	Normal Renal Cortex (Mean Values)
MIP	HU	153.9	159.1
BF	ml/100 ml/min	284.8	410.5
BV	ml/1000 ml ml/100ml	203.7 20.37	290.3 29.03
PMB	0.5 ml/100ml/min ml/100ml/min	162.3 81.15	208.3 104.15

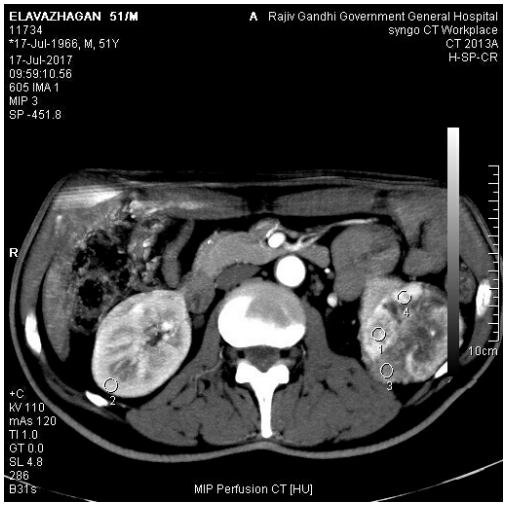
The solid component of the lesion showed higher blood flow, blood volume and permeability than the cystic component, but reduced values when compared to that of the normal renal cortex.

HPE – CLEAR CELL RENAL CELL CARCINOMA (LOW GRADE)

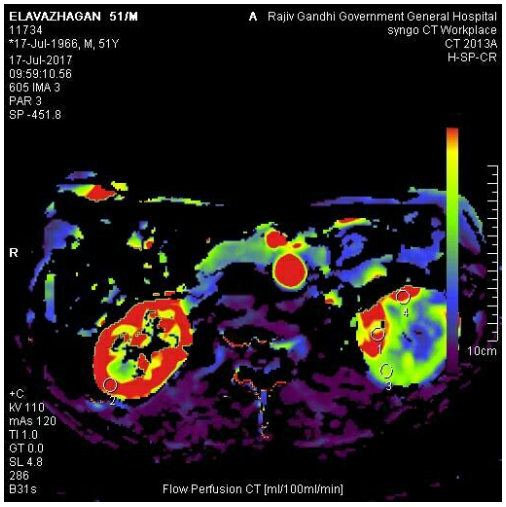


CASE 2

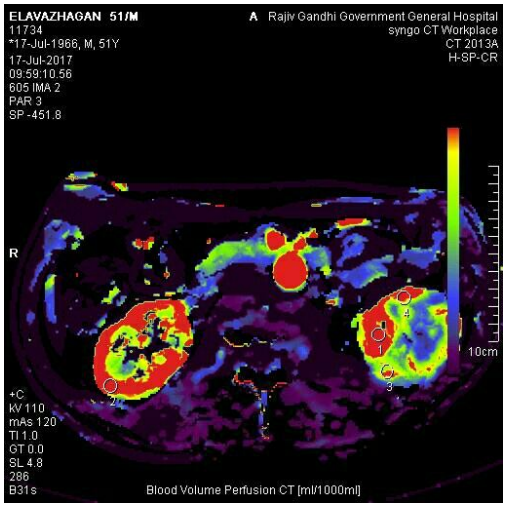
History: 51 years old male patient presented with 3 episodes of hematuria, was diagnosed with a left lower pole, hypervascular renal lesion.



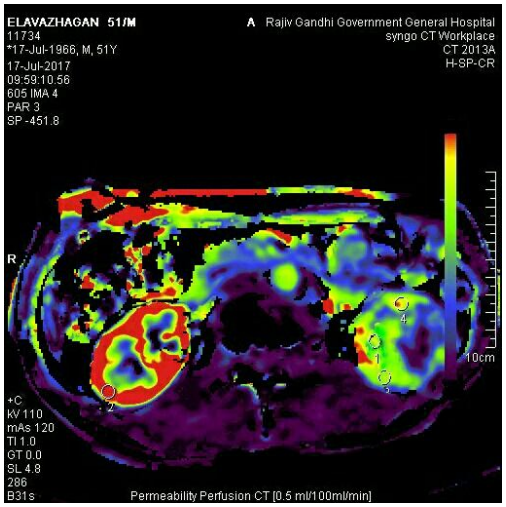
MIP PERFUSION CT (HU)



BLOOD FLOW (BF)



BLOOD VOLUME (BV)



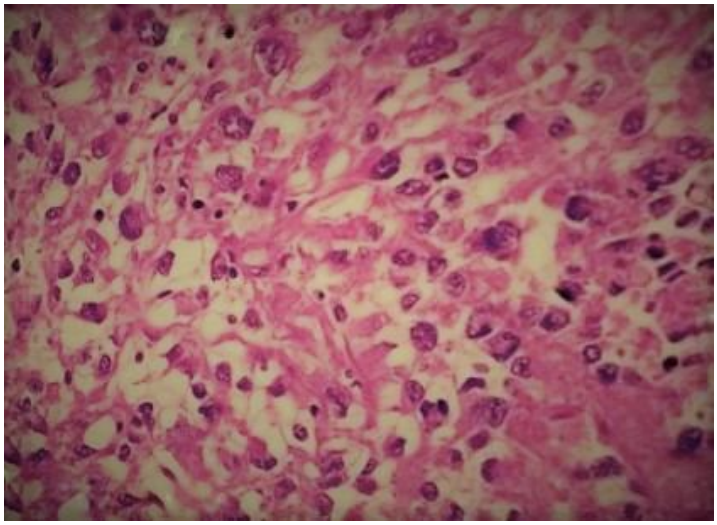
PERMEABILITY (PMB)

CT Perfusion Interpretation:

Parameters	Unit	Within the lesion (Mean Values)	Normal Renal Cortex (Mean Values)
MIP	HU	146.3	161.9
BF	ml/100 ml/min	378.4	436.9
BV	ml/1000 ml ml/100ml	270.3 27.03	299.2 29.92
PMB	0.5 ml/100ml/min ml/100ml/min	176.2 88.1	211.9 105.9

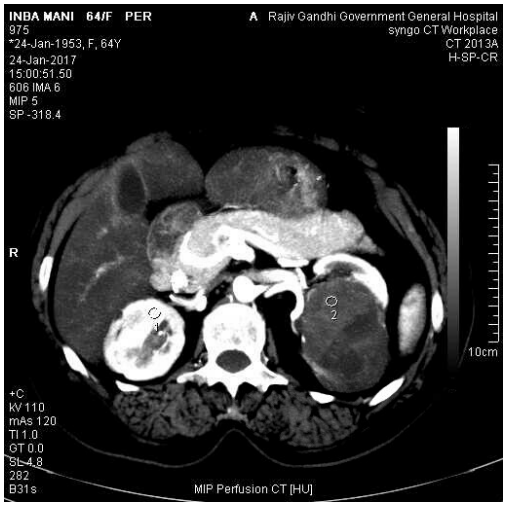
The lesion showed higher blood flow, blood volume and permeability but lesser than that of the normal renal cortex.

HPE – CLEAR CELL RENAL CELL CARCINOMA (HIGH GRADE)

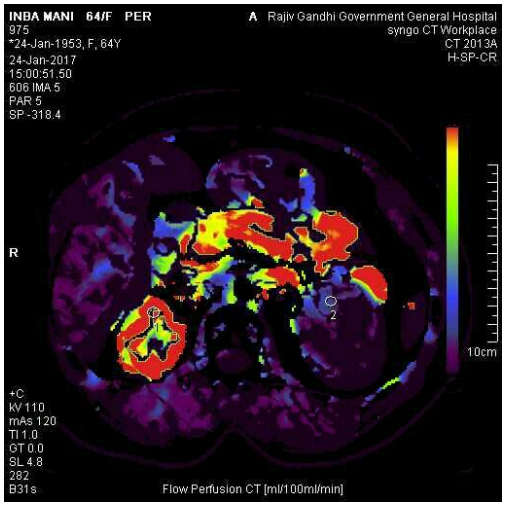


CASE 3

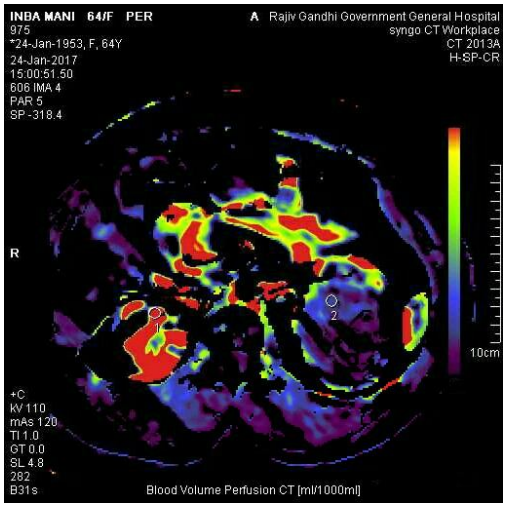
History: 64 years old female patient with left loin pain, diagnosed with a left renal hypovascular lesion.



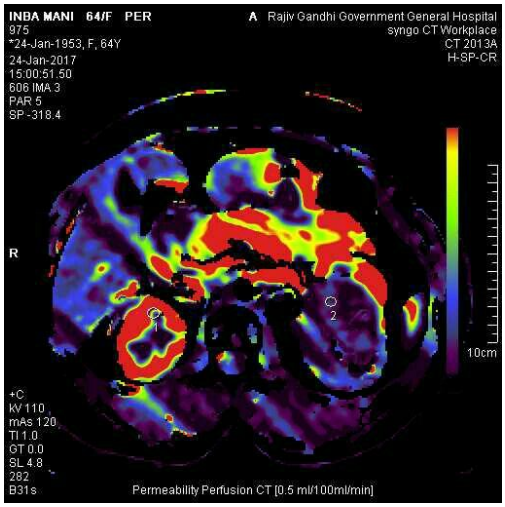
MIP PERFUSION CT (HU)



BLOOD FLOW (BF)



BLOOD VOLUME (BV)



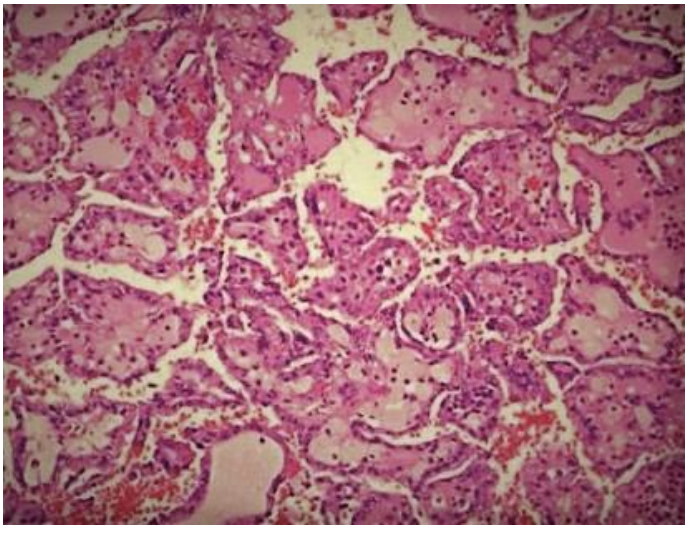
PERMEABILITY (PMB)

CT Perfusion Interpretation:

Parameters	Unit	Within the lesion (Mean Values)	Normal Renal Cortex (Mean Values)
MIP	HU	67.1	164.8
BF	ml/100 ml/min	90	380.7
BV	ml/1000 ml ml/100ml	81.2 8.12	321.1 32.11
PMB	0.5 ml/100ml/min ml/100ml/min	53.5 26.75	200.1 100.1

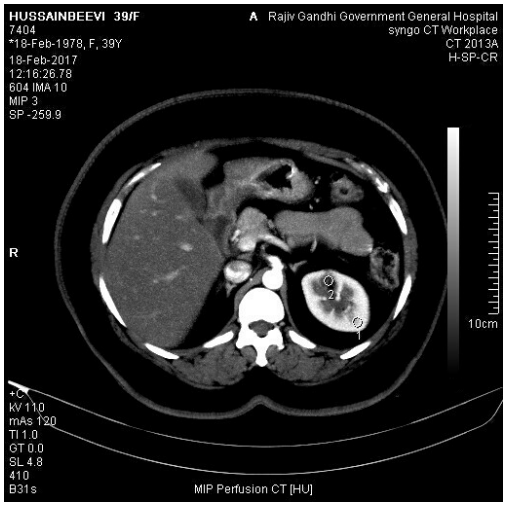
The lesion showed markedly decreased blood flow, blood volume and permeability values compared to that of the normal renal cortex.

HPE – PAPILLARY RENAL CELL CARCINOMA

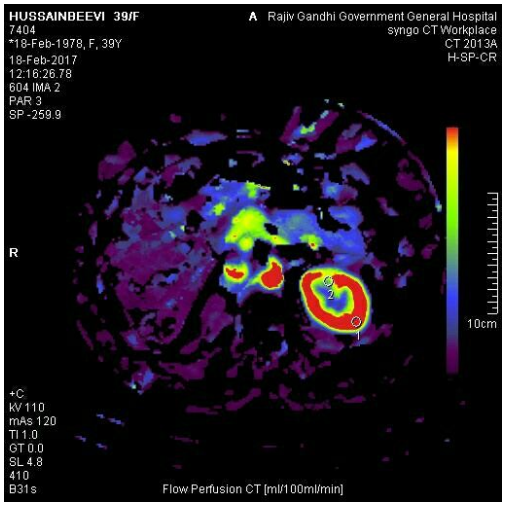


CASE 4

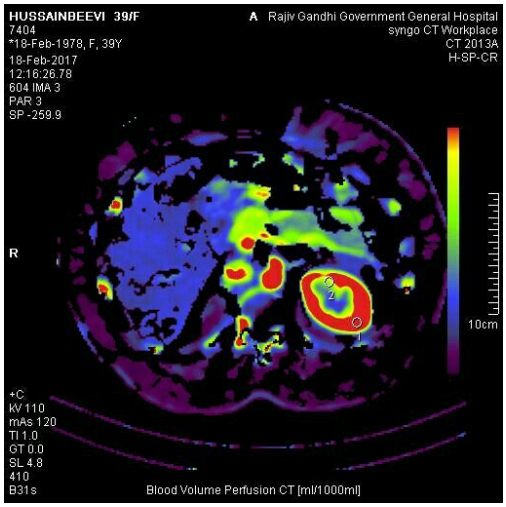
History: 39 years old female patient incidentally diagnosed with a left upper pole, hypovascular renal lesion.



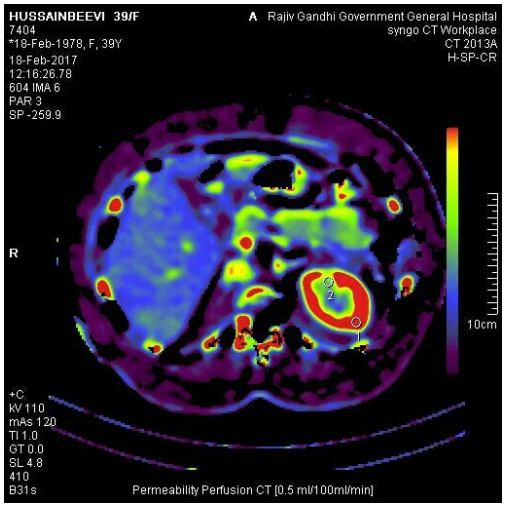
MIP PERFUSION CT (HU)



BLOOD FLOW (BF)



BLOOD VOLUME (BV)



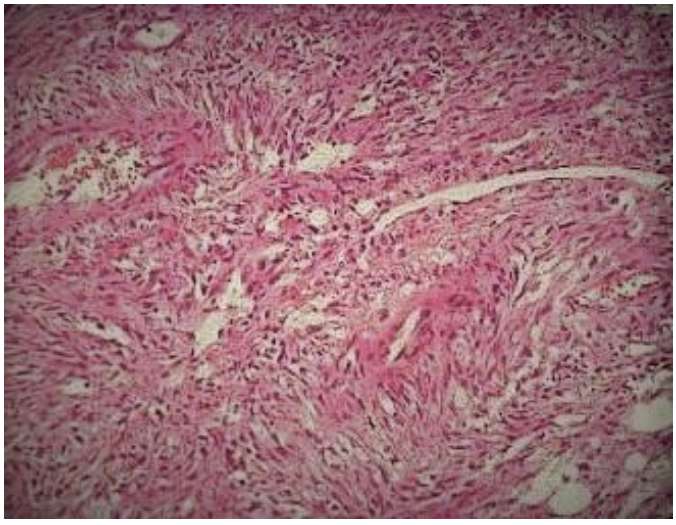
PERMEABILITY (PMB)

CT Perfusion Interpretation:

Parameters	Unit	Within the lesion (Mean Values)	Normal Renal Cortex (Mean Values)
MIP	HU	99.5	168.5
BF	ml/100 ml/min	239.7	377.8
BV	ml/1000 ml ml/100ml	133.4 13.34	260.7 26.07
PMB	0.5 ml/100ml/min ml/100ml/min	88.1 44.05	194.1 97.05

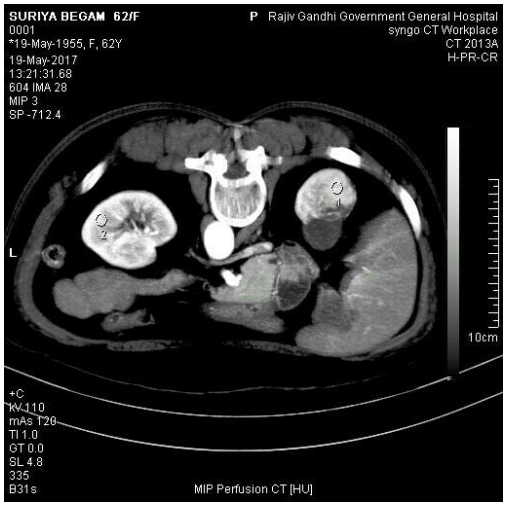
The lesion showed significantly lower values of blood flow, blood volume and permeability compared to that of the normal renal cortex.

HPE – ANGIOMYOLIPOMA WITH MINIMAL FAT

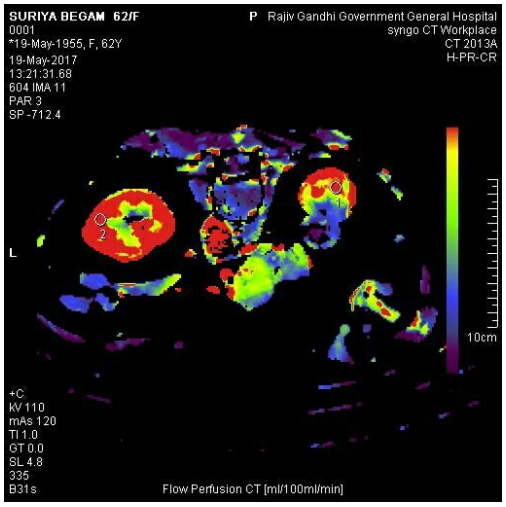


CASE 5

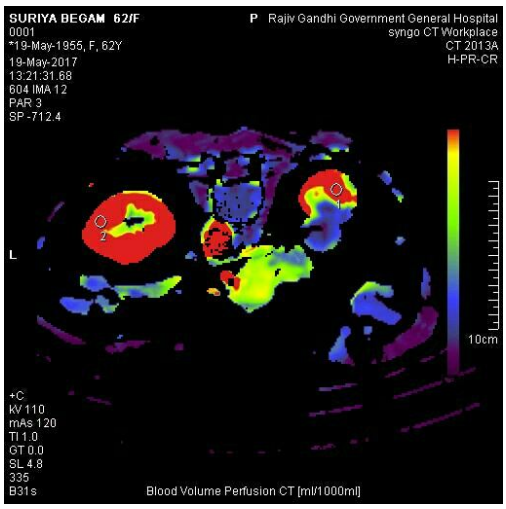
History: 62 years old female patient with right loin pain diagnosed with a right upper pole, hypervascular renal lesion, with an adjacent simple cortical cyst.



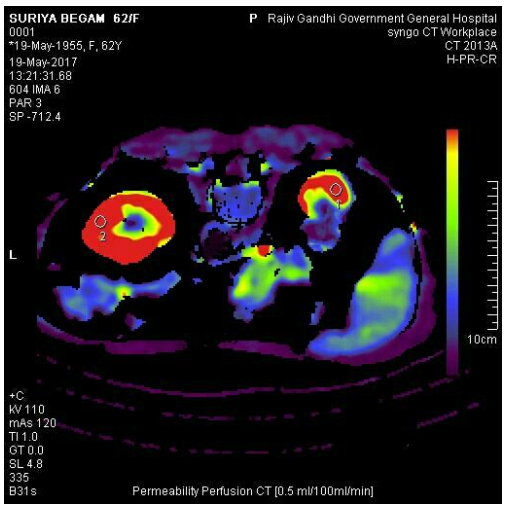
MIP PERFUSION CT (HU)



BLOOD FLOW (BF)



BLOOD VOLUME (BV)



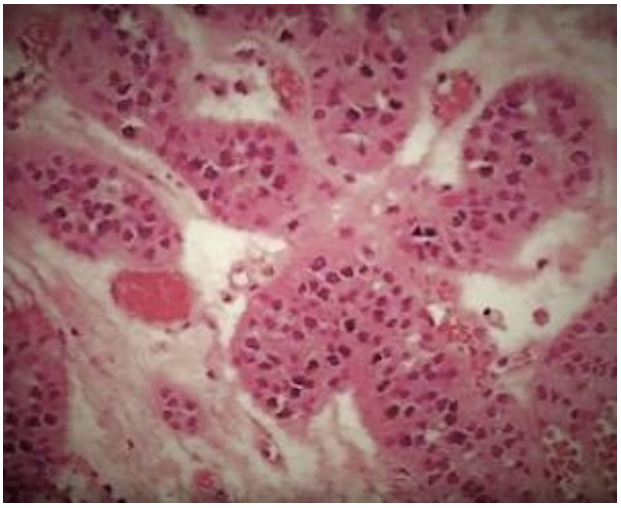
PERMEABILITY (PMB)

CT Perfusion Interpretation:

Parameters	Unit	Within the lesion (Mean Values)	Normal Renal Cortex (Mean Values)
MIP	HU	171.4	164
BF	ml/100 ml/min	408	430.3
BV	ml/1000 ml ml/100ml	326.9 32.69	316.9 31.69
PMB	0.5 ml/100ml/min ml/100ml/min	202.1 101.05	200.3 100.15

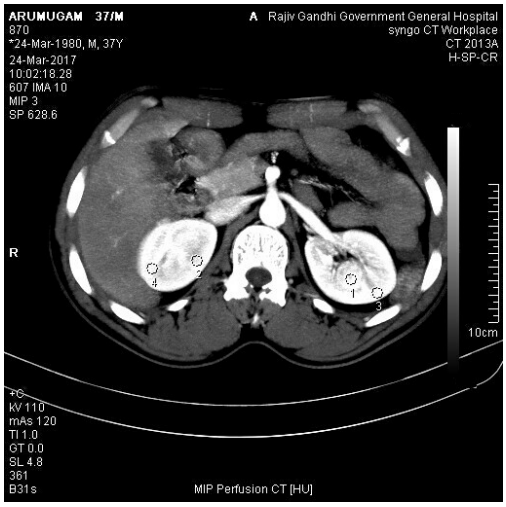
The lesion showed higher blood flow, blood volume and permeability more or less similar to that of the normal renal cortex.

HPE – ONCOCYTOMA

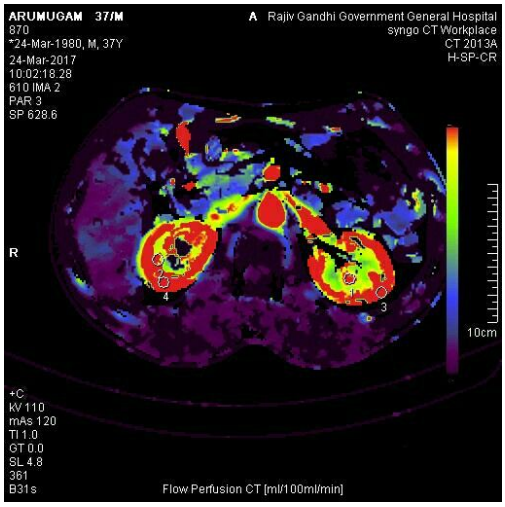


CASE 6

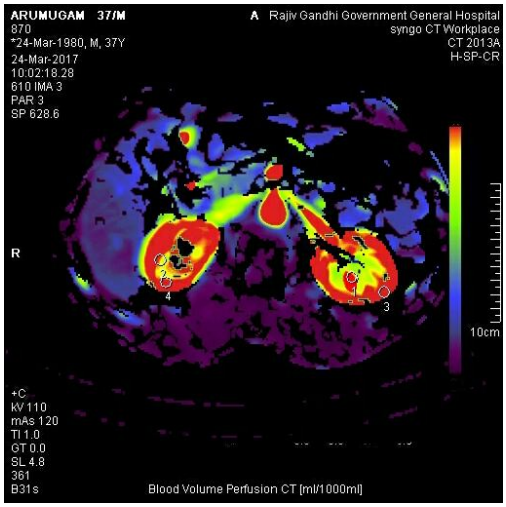
History: 37 years old male patient incidentally diagnosed with a left hypervascular renal lesion.



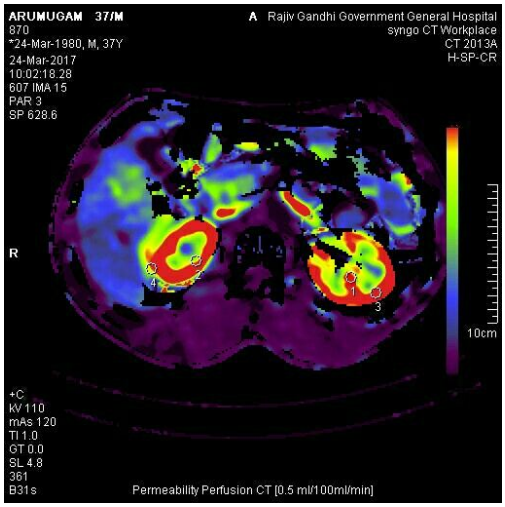
MIP PERFUSION CT (HU)



BLOOD FLOW (BF)



BLOOD VOLUME (BV)



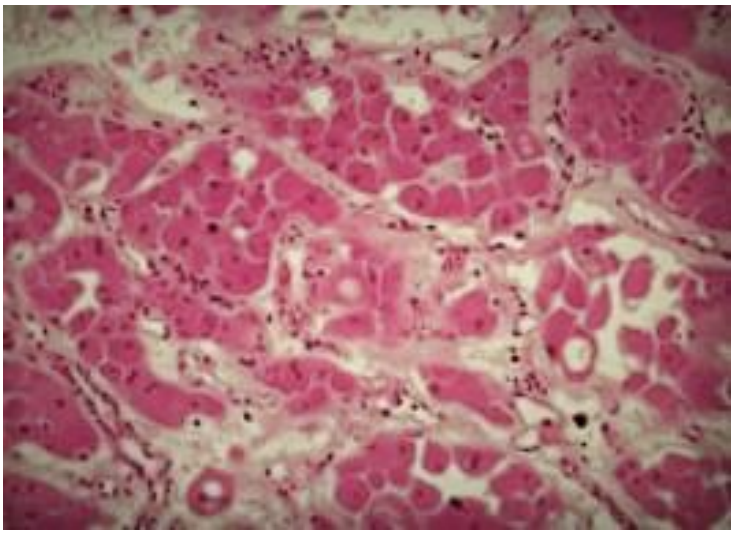
PERMEABILITY (PMB)

CT Perfusion Interpretation:

Parameters	Unit	Within the lesion (Mean Values)	Normal Renal Cortex (Mean Values)
MIP	HU	175.2	169
BF	ml/100 ml/min	382.3	387
BV	ml/1000 ml ml/100ml	261.3 26.13	260.5 26.05
PMB	0.5 ml/100ml/min ml/100ml/min	232.1 116.05	211.9 105.95

The lesion showed higher blood flow, blood volume and permeability almost equal to that of the normal renal cortex values.

HPE – ONCOCYTOMA



Statistical analysis

6. STATISTICAL ANALYSIS

The collected data from all the enrolled patients were analysed with IBM.SPSS statistics software 23.0 Version.

To describe about the data descriptive statistics, frequency analysis, percentage analysis were used for categorical variables and the mean & Standard Deviation were used for continuous variables.

To find the significant difference between the bivariate samples in Paired groups, the Paired sample t-test was used & for Independent groups, the Unpaired sample t-test was used.

For the multivariate analysis the one way ANOVA with Tukey's Post-Hoc test was used.

The Receiver Operating Curve (ROC) was used to assess the Cut-Off values, Sensitivity, Specificity, positive predictive value and negative predictive value.

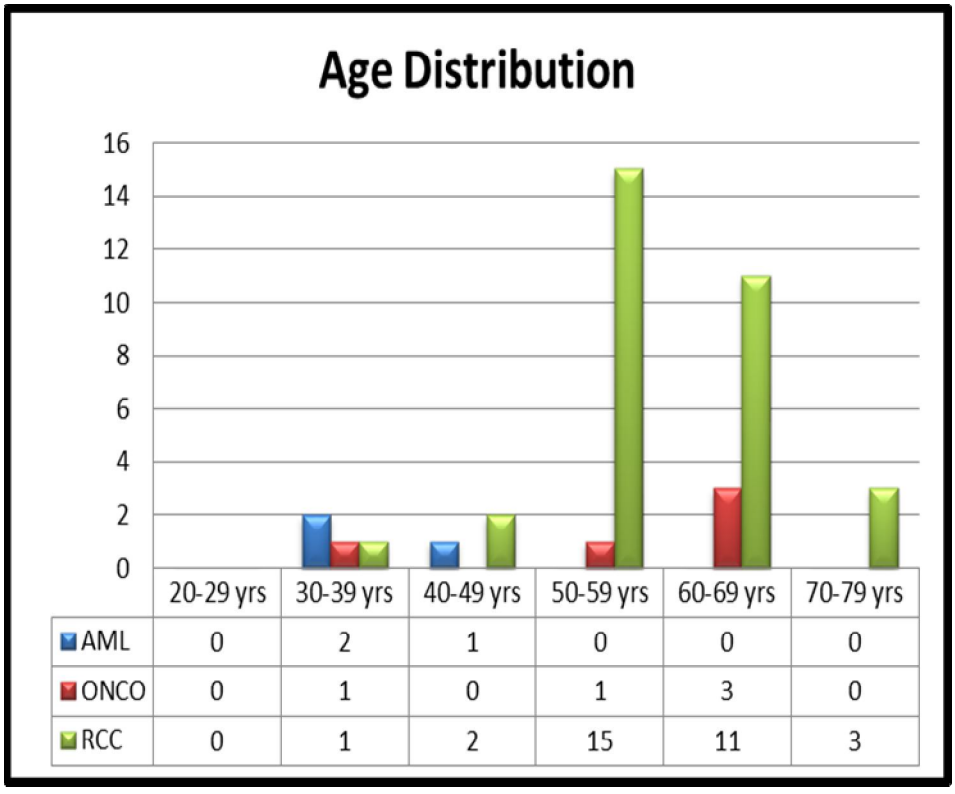
In all the above statistical tools the probability value .05 is considered as significant level.

Observation and results

7. OBSERVATION & RESULTS

7.1 AGE RANGE DISTRIBUTION

In this study, renal cell carcinomas were more common in 6th and 7th decades (81%), whereas AML were more common in 4th decade (66%) and oncocytomas in 7th decade (60%).



	20-29 yrs	30-39 yrs	40-49 yrs	50-59 yrs	60-69 yrs	70-79 yrs
AML	0	2	1	0	0	0
ONCO	0	1	0	1	3	0
RCC	0	1	2	15	11	3

Fig: 7.1.1 Bar diagram showing the age range distribution of different renal lesions among the study group.

7.2 GENDER DISTRIBUTION

In this study, out of 40 patients, 24 were males (60%) and 16 were females(40%) .

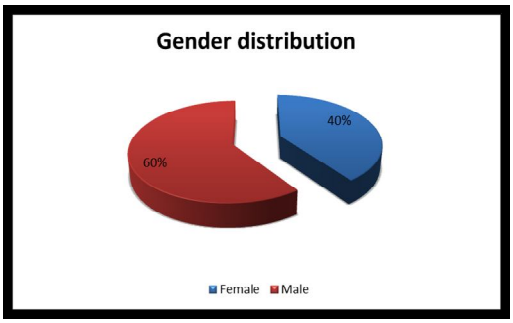


Fig :7.2.1 Pie chart showing gender distribution of renal lesions among the study group

Out of 32 patients of renal cell carcinoma 21(65.6%) were males and 11 were females(34.4%). In patients with oncocytoma 3 were males(60%) and 2 were females(40%). In AML with minimal fat all 3 were females.

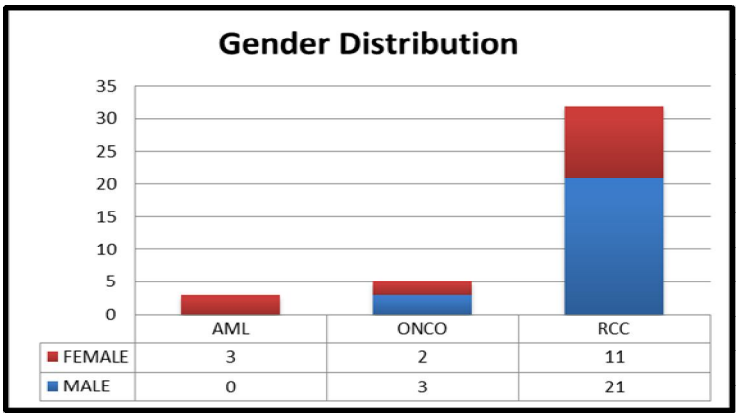


Fig: 7.2.2 Bar diagram showing gender distribution of different renal lesions among the study group

7.3 FREQUENCY DISTRIBUTION OF RENAL LESIONS IN HISTOPATHOLOGY

Out of the 40 renal lesions among the study group, 32 were RCCs (80%), 5 were Oncocytomas (13%), and 3 were AML with minimal fat(7%). Out of the 32 lesions which were found to be RCC, 21 were clear cell RCC (80%), 6 were chromophobe RCC (19%), 4 were Papillary RCC (12%), 1 was poorly differentiated RCC(3%). And among the clear cell RCC, 11 were of low grade (52%) and 10 were of high grade(48%).

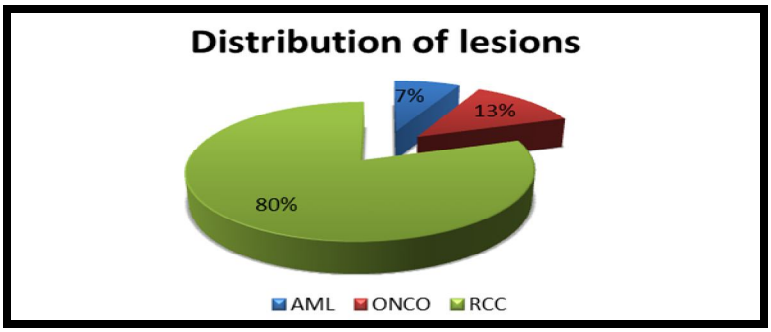


Fig :7.3.1 Pie chart showing the distribution of histopathological types of renal lesions among the study group

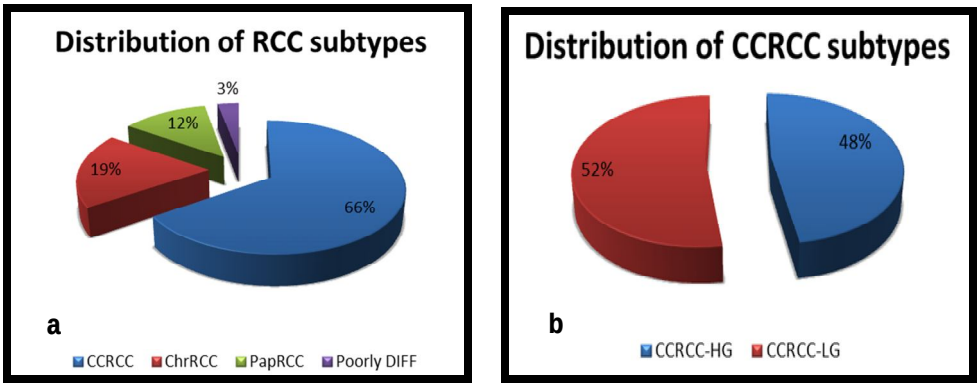


Fig: 7.3.2 Pie charts showing (a) the distribution of subtypes of RCC and (b) grading of clear cell RCC

HISTOPATHOLOGICAL DIAGNOSIS	Frequency	Percent	Valid Percent	Cumulative Percent
AML with minimal fat	3	7.5	7.5	7.5
Oncocytoma	5	12.5	12.5	20
Clear cell RCC - High Grade	10	25	25	45
Clear cell RCC - Low Grade	11	27.5	27.5	72.5
Papillary type RCC	4	10	10	82.5
Chromophobe type RCC	6	15	15	97.5
Poorly differentiated adenocarcinoma	1	2.5	2.5	100
Total	**40**	**100**	**100**	

Table: 7.3.1 Table showing overall frequency distribution of histopathological types and subtypes of renal lesions in the study group

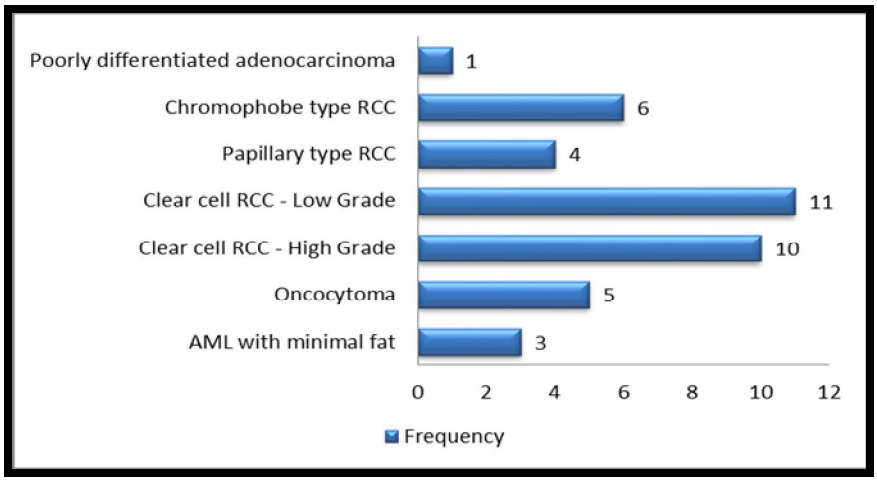


Fig : 7.3.3 Bar diagram showing overall distribution of various histopathological types and subtypes of renal lesions among the study group

7.4 CROSS TABULATIONS – SIDE, LOCATION, ENHANCEMENT

The tables below show the distribution of the renal lesions according to the side of the kidney involved, location of the lesion within the kidney and the CT characteristics based on the enhancement.

		Side		
		Left	Right	Total
GROUPS	AML	3	0	3
	ONCO	2	3	5
	RCC	21	11	32
Total		26	14	40

Table: 7.4.1 Cross tabulation showing the side of the kidney involved

		Location			
		LP	Mid	UP	Total
GROUPS	AML	1	1	1	3
	ONCO	1	2	2	5
	RCC	9	17	6	32
Total		11	20	9	40

Table: 7.4.2 Cross tabulation showing the location of the lesion within the kidney

		CT characteristics			
		HN	HO	HR	Total
GROUPS	AML	0	2	1	3
	ONCO	1	0	4	5
	RCC	10	8	14	32
Total		11	10	19	40

Table: 7.4.3 Cross tabulation showing the CT characteristics of the lesion based on the enhancement (hypervascular - HR, hypervascular with necrosis - HN, hypovascular - HO)

7.5 MEAN VALUES OF CT PERFUSION PARAMETERS AMONG THE RENAL LESIONS - GROUP STATISTICS

		N	Mean Values	Std. Deviation	Std. Error	95% Confidence Interval for Mean		Minimum	Maximum
						Lower Bound	Upper Bound		
BF-RL	AML	3	241.400	9.5640	5.5218	217.642	265.158	232.8	251.7
	ONCO	5	404.720	25.1488	11.2469	373.494	435.946	375.7	431.5
	RCC	32	260.722	90.1616	15.9385	228.215	293.229	90.0	383.2
	Total	40	277.273	94.5375	14.9477	247.038	307.507	90.0	431.5
BV-RL	AML	3	129.733	8.8867	5.1307	107.658	151.809	119.6	136.2
	ONCO	5	297.820	33.3003	14.8923	256.472	339.168	261.3	326.9
	RCC	32	191.191	65.7542	11.6238	167.484	214.898	76.4	281.4
	Total	40	199.910	72.2823	11.4288	176.793	223.027	76.4	326.9
PMB-RL	AML	3	82.533	8.1329	4.6955	62.330	102.736	73.2	88.1
	ONCO	5	203.480	22.8263	10.2083	175.137	231.823	175.4	232.1
	RCC	32	99.500	41.1632	7.2767	84.659	114.341	40.6	179.6
	Total	40	111.225	51.6812	8.1715	94.697	127.753	40.6	232.1

Table: 7.5.1 Table showing intralesional mean values of Blood Flow, Blood Volume, Permeability among the various renal lesions in the study group

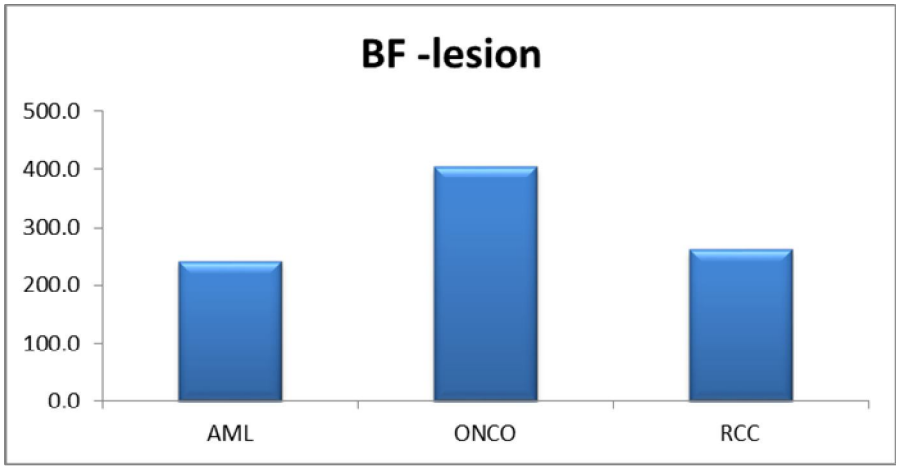


Fig: 7.5.1 Bar diagram showing mean values of intralesional blood flow (BF) in various renal lesions among the study group

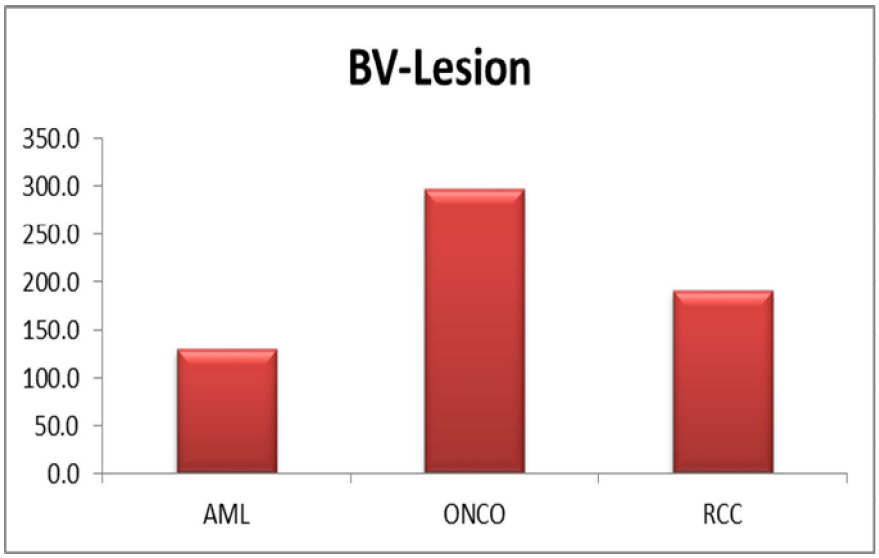


Fig: 7.5.2 Bar diagram showing mean values of intralesional blood volume(BV) in various renal lesions among the study group

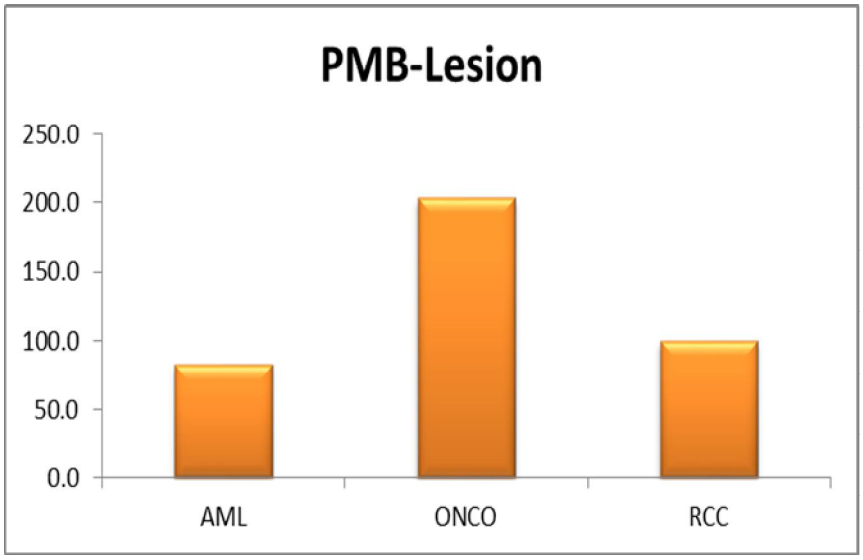


Fig: 7.5.3 Bar diagram showing mean values of intralesional permeability (PMB) in various renal lesions among the study group

COMPARISON BY ANOVA AND TUKEY POST HOC TESTS

BY ANOVA TEST		Sig. P- value
BF-RL	Between Groups	.003
	Within Groups	
BV-RL	Between Groups	.001
	Within Groups	
PMB-RL	Between Groups	.000
	Within Groups	

Table: 7.5.2 Anova Test shows significant differences among the values of CT perfusion paramters in various renal lesions.

Tukey Post Hoc test Dependent Variable			Mean Difference (I-J)	Std. Error	Sig. P- value
BF-RL	AML	ONCO	-163.3200*	60.5935	.028
	AML	RCC	-19.3219	50.0986	.921
	ONCO	RCC	143.9981*	39.8995	.003
BV-RL	AML	ONCO	-168.0867*	44.7013	.002
	AML	RCC	-61.4573	36.9589	.233
	ONCO	RCC	106.6294*	29.4348	.002
PMB-RL	AML	ONCO	-120.9467*	28.0908	.000
	AML	RCC	-16.9667	23.2254	.747
	ONCO	RCC	103.9800*	18.4972	.000

Table:7.5.3 Tukey HSD post Hoc Test shows significant differences in BF,BV,PMB in oncocytomas vs RCC and AML, whereas no significant difference was seen between AML and RCC.

P - Value	** Highly Significant at P ≤ .01
P - Value	* Significant at 0.01 < P ≤ .05
P -Value	# Not Significant P >.05

7.6 MEAN VALUES OF CTP PARAMETERS OF AML, CLEAR CELL RCC & NON CLEAR CELL RCC - GROUP STATISTICS

		N	Mean Values	Std. Deviation	Std. Error	95% Confidence Interval for Mean		Minimum	Maximum
						Lower Bound	Upper Bound		
BF-RL	AML	3	241.400	9.5640	5.5218	217.642	265.158	232.8	251.7
	CCRCC	22	314.523	43.4519	9.2640	295.257	333.788	248.1	383.2
	NON CCRCC	10	142.360	30.8732	9.7630	120.275	164.445	90.0	169.4
	Total	35	259.066	86.2980	14.5870	229.421	288.710	90.0	383.2
BV-RL	AML	3	129.733	8.8867	5.1307	107.658	151.809	119.6	136.2
	CCRCC	22	231.264	28.7918	6.1384	218.498	244.029	197.2	281.4
	NON CCRCC	10	103.030	19.9222	6.2999	88.779	117.281	76.4	143.2
	Total	35	185.923	65.2032	11.0214	163.525	208.321	76.4	281.4
PMB-RL	AML	3	82.533	8.1329	4.6955	62.330	102.736	73.2	88.1
	CCRCC	22	118.305	35.3743	7.5418	102.620	133.989	79.2	179.6
	NON CCRCC	10	58.130	12.2677	3.8794	49.354	66.906	40.6	83.2
	Total	35	98.046	39.6487	6.7019	84.426	111.666	40.6	179.6

Table: 7.6.1 Table showing intralesional mean values of Blood Flow, Blood Volume, Permeability in angiomyolipomas, clear cell RCCs and other RCCs in the study group

COMPARISON BY TUKEY POST HOC TESTS

Tukey Post Hoc test Dependent Variable			Mean Difference (I-J)	Std. Error	Sig. P- value
BF-RL	AML	CCRCC	-73.1227*	23.9383	.012
		NON CCRCC	99.0400*	25.6039	.001
BV-RL	AML	CCRCC	-101.5303*	15.8182	.000
		NON CCRCC	26.7033	16.9188	.269
PMB-RL	AML	CCRCC	-35.7712	18.1289	.135
		NON CCRCC	24.4033	19.3903	.428

Table: 7.6.2 Tukey HSD post Hoc Test shows significant differences in both BF and BV between AML and Clear cell RCC, significant difference only in BF between AML and other RCC subtypes, whereas no significant differences were found in permeability values between the lesions.

7.7 MEAN VALUES OF CT PERFUSION PARAMETERS AMONG THE RENAL CELL CARCINOMA SUBTYPES - GROUP STATISTICS

		N	Mean Values	Std. Deviation	Std. Error	95% Confidence Interval for Mean		Minimum	Maximum
						Lower Bound	Upper Bound		
BF-RL	CCRCC	21	315.967	43.9807	9.5974	295.947	335.986	248.1	383.2
	ChrRCC	6	160.517	7.3890	3.0166	152.762	168.271	147.5	169.4
	PapRCC	4	115.125	33.4685	16.7343	61.869	168.381	90.0	164.3
	Total	31	259.965	91.5485	16.4426	226.384	293.545	90.0	383.2
BV-RL	CCRCC	21	232.186	29.1680	6.3650	218.909	245.463	197.2	281.4
	ChrRCC	6	112.467	16.7400	6.8341	94.899	130.034	97.3	143.2
	PapRCC	4	88.875	16.6848	8.3424	62.326	115.424	76.4	113.4
	Total	31	190.523	66.7306	11.9852	166.046	215.000	76.4	281.4
PMB-RL	CCRCC	21	120.110	35.1944	7.6800	104.089	136.130	79.2	179.6
	ChrRCC	6	58.467	12.8081	5.2289	45.025	71.908	47.1	83.2
	PapRCC	4	57.625	13.3233	6.6616	36.425	78.825	40.6	69.2
	Total	31	100.116	41.6934	7.4884	84.823	115.409	40.6	179.6

Table: 7.7.1 Table showing intralesional mean values of Blood Flow, Blood Volume, Permeability among the RCC types in the study group

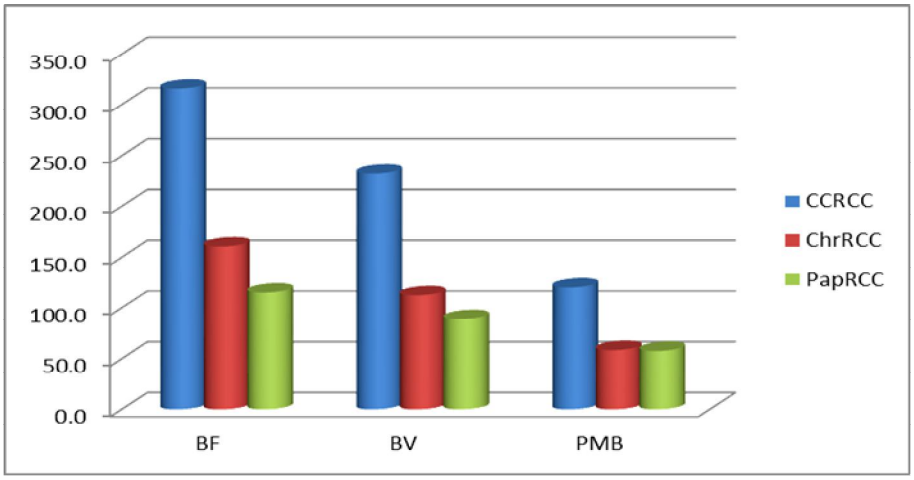


Fig: 7.7.1 Bar diagram showing intralesional mean values of Blood Flow, Blood Volume, Permeability among the RCC types in the study group

COMPARISON BY TUKEY POST HOC TESTS:

Tukey Post Hoc test Dependent Variable			Mean Difference (I-J)	Std. Error	Sig. P- value
BF-RL	CCRCC	ChrRCC	155.4500*	17.9965	.000
	CCRCC	PapRCC	200.8417*	21.2091	.000
	ChrRCC	PapRCC	45.3917	25.0949	.185
BV-RL	CCRCC	ChrRCC	119.7190*	12.1382	.000
	CCRCC	PapRCC	143.3107*	14.3050	.000
	ChrRCC	PapRCC	23.5917	16.9258	.358
PMB-RL	CCRCC	ChrRCC	61.6429*	14.1401	.000
	CCRCC	PapRCC	62.4845*	16.6642	.002
	ChrRCC	PapRCC	.8417	19.7174	.999

Table: 7.7.2 Tukey HSD post Hoc Test shows significant differences in BF,BV,PMB in Clear cell RCC vs Chromophobe RCC and Papillary RCC, whereas no significant difference was seen between Chromophobe RCC and Papillary RCC.

7.8 MEAN VALUES OF CT PERFUSION PARAMETERS IN CLEAR CELL RCC HIGH GRADE VS LOW GRADE - GROUP STATISTICS

SUBGROUPS		N	Mean	Std. Deviation	Std. Error Mean
BF-RL	CCRCC-LG	11	292.827	44.5546	13.4337
	CCRCC-HG	10	341.420	26.8049	8.4764
BV-RL	CCRCC-LG	11	214.645	26.3413	7.9422
	CCRCC-HG	10	251.480	18.1655	5.7444
PMB-RL	CCRCC-LG	11	122.127	32.7571	9.8766
	CCRCC-HG	10	117.890	39.3680	12.4493

Table: 7.8.1 Table showing intralesional mean values of Blood Flow, Blood Volume, Permeability among the high grade and low grade clear cell RCC's in the study group

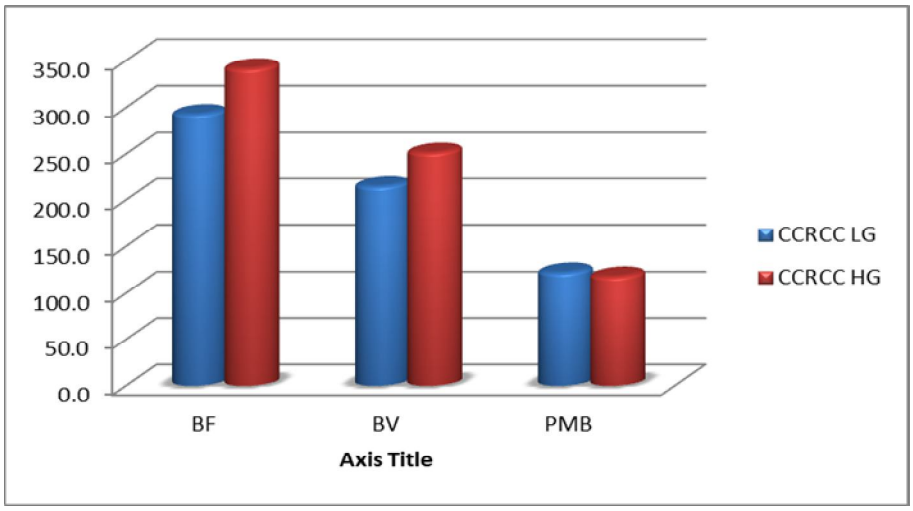


Fig: 7.8.1 Bar diagram showing intralesional mean values of Blood Flow, Blood Volume, Permeability in low grade and high grade clear cell renal cell carcinoma

COMPARISON BY INDEPENDENT SAMPLES T-TEST

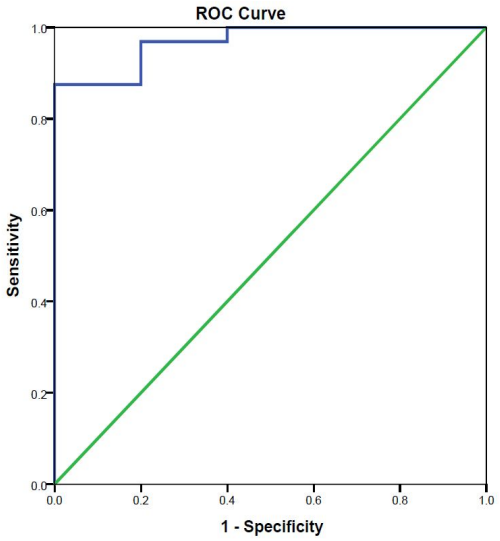
		Levene's Test for Equality of Variances		t-test for Equality of Means		
		F	Sig.	t	df	Sig. (2-tailed)
BF-RL	Equal variances assumed	1.151	.297	-2.988	19	.008
	Equal variances not assumed			-3.059	16.621	.007
BV-RL	Equal variances assumed	.346	.563	-3.692	19	.002
	Equal variances not assumed			-3.758	17.790	.001
PMB-RL	Equal variances assumed	1.191	.289	.269	19	.791
	Equal variances not assumed			.267	17.614	.793

Table:.7.8.2 Unpaired independent sample T - Test shows significant differences in BF,BV in high grade Clear cell RCC vs low grade Clear cell RCC whereas no significant difference was seen in PMB between them.

7.9 ROC CURVE ANALYSIS (RCC AND ONCOCYTOMA)

BLOOD FLOW (BF)

The cut off value of BF obtained by ROC curve analysis from our study along with the Sensitivity, Specificity, Positive Predictive Value (PPV) And Negative Predictive Value (NPV) to differentiate RCC and Oncocytomas are as below.



SENSITIVITY	87.50%
SPECIFICITY	100.00%
PPV	100.00%
NPV	55.56%

Area Under the Curve

Test Result Variable(s): BF-RL

Area	Std. Error[a]	Asymptotic Sig.[b]	Asymptotic 95% Confidence Interval	
			Lower Bound	Upper Bound
.969	.029	.001	.912	1.000

a. Under the nonparametric assumption

b. Null hypothesis: true area = 0.5

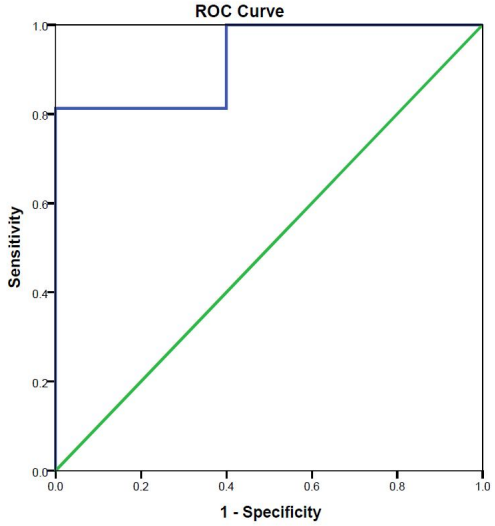
CUT OFF VALUE: 366.2 ml/100ml/min

		GROUPS		
	ml /100 ml/min	RCC	ONCO	Total
BF-RL	<= 366.2	28	0	29
	>366.2	4	5	8
Total		32	5	37

Fig: 7.9.1 ROC curve analysis for Blood Flow (RCC vs Oncocytoma)

BLOOD VOLUME (BV)

The cut off value of BV obtained by ROC curve analysis from our study along with the Sensitivity, Specificity, PPV, NPV to differentiate RCC and Oncocytomas are as below.



SENSITIVITY	81.30%
SPECIFICITY	100.00%
PPV	100.00%
NPV	45.45%

Area Under the Curve

Test Result Variable(s): BV-RL

Area	Std. Error[a]	Asymptotic Sig.[b]	Asymptotic 95% Confidence Interval	
			Lower Bound	Upper Bound
.925	.052	.003	.824	1.000

a. Under the nonparametric assumption

b. Null hypothesis: true area = 0.5

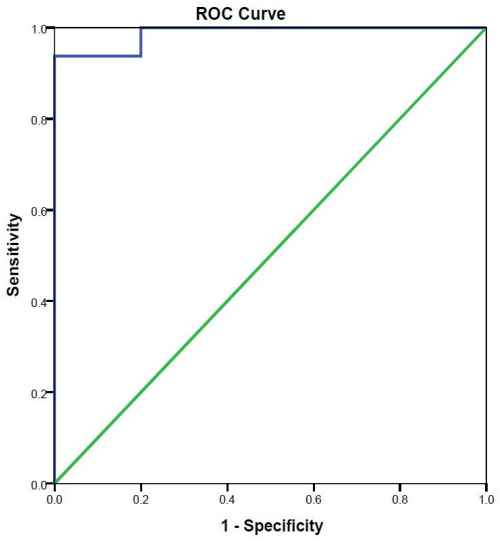
CUT OFF VALUE: 254.8 ml/1000 ml (OR) 25.48 ml/100 ml

		GROUPS		
	ml/1000ml	RCC	ONCO	Total
BV-RL	<= 254.8	26	0	27
	> 254.8	6	5	10
Total		32	5	37

Fig: 7.9.2 ROC curve analysis for Blood Volume (RCC vs Oncocytoma)

PERMEABILITY (PMB)

The cut off value of PMB obtained by ROC curve analysis from our study along with the Sensitivity, Specificity, PPV, NPV to differentiate RCC and Oncocytomas are as below.



SENSITIVITY	93.80%
SPECIFICITY	100%
PPV	100%
NPV	71%

Area Under the Curve

Test Result Variable(s): PMB-RL

Area	Std. Error[a]	Asymptotic Sig.[b]	Asymptotic 95% Confidence Interval	
			Lower Bound	Upper Bound
.988	.016	.001	.956	1.000

a. Under the nonparametric assumption

b. Null hypothesis: true area = 0.5

CUT OFF VALUE: 174.8 (0.5ml/100ml/min) OR 87.4 (ml/100ml/min)

	0.5 ml/100 ml/min	GROUPS		Total
		RCC	ONCO	
PMB-RL	<= 174.8	30	0	30
	> 174.8	2	5	7
Total		32	5	37

Fig: 7.9.3 ROC curve analysis for Permeability (RCC vs Oncocytoma)

7.10 NORMAL RENAL CORTEX VS INTRALESIONAL VALUES

ONCOCYTOMA AND NORMAL RENAL CORTEX

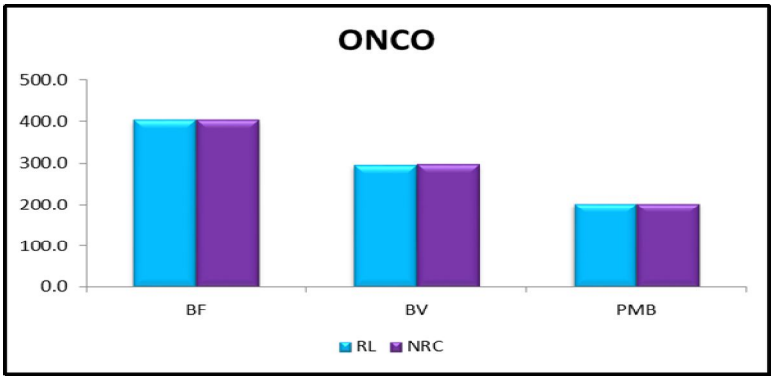


Fig: 7.10.1 Bar diagram showing intralesional mean values of Blood Flow, Blood Volume, Permeability of oncocytomas in the study group in comparison with normal renal cortex mean values

Paired Samples Test (Oncocytoma vs normal renal cortex)

	Paired Differences					t	Df	Sig. (2-tailed)
	Mean	SD	Std. Error Mean	95% Confidence Interval of the Difference				
				Lower	Upper			
BF-RL – BF-NRC	.6400	27.83	12.4445	-33.9114	35.1914	.051	4	.961
BV-RL - BV-NRC	-1.2000	19.63	8.7775	-25.5703	23.1703	-.137	4	.898
PMB-RL - PMB-NRC	-1.4800	19.21	8.5922	-25.3357	22.3757	-.172	4	.872

Table:7.10.1 Paired samples Test shows no significant differences(P>0.05) between the intralesional mean values of Blood Flow, Blood Volume, Permeability of oncocytomas in the study group in comparison with normal renal cortex mean values

ANGIOMYOLIPOMA AND NORMAL RENAL CORTEX

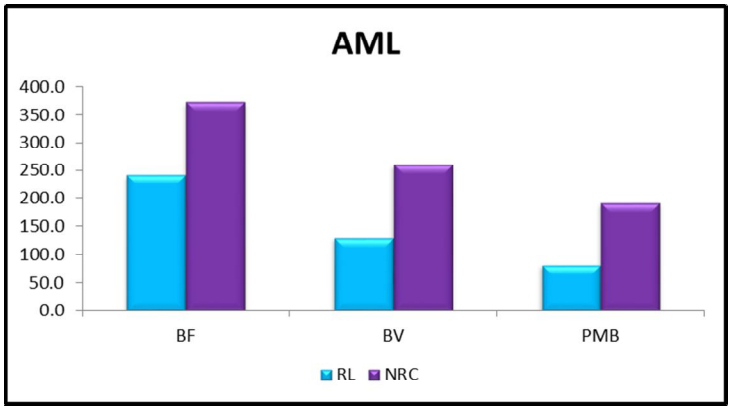


Fig: 7.10.2 Bar diagram showing intralesional mean values of Blood Flow, Blood Volume, Permeability of angiomyolipomas in the study group in comparison with normal renal cortex mean values.

Paired Samples Test (Angiomyolipoma vs normal renal cortex)

	Paired Differences					t	Df	Sig. (2-tailed)
	Mean	SD	Std. Error Mean	95% Confidence Interval of the Difference				
				Lower	Upper			
BF-RL – BF-NRC	-131.50	13.84	7.99	-165.8701	-97.1299	-16.462	2	.004
BV-RL - BV-NRC	-130.70	8.62	4.98	-152.1098	-109.2902	-26.266	2	.001
PMB-RL - PMB-NRC	-109.70	3.24	1.86	-117.7380	-101.6620	-58.721	2	.000

Table:7.10.2 Paired samples Test shows significant differences (P<0.01) between the intralesional mean values of Blood Flow, Blood Volume, Permeability of angiomyolipomas in the study group in comparison with normal renal cortex mean values

RENAL CELL CARCINOMA AND NORMAL RENAL CORTEX

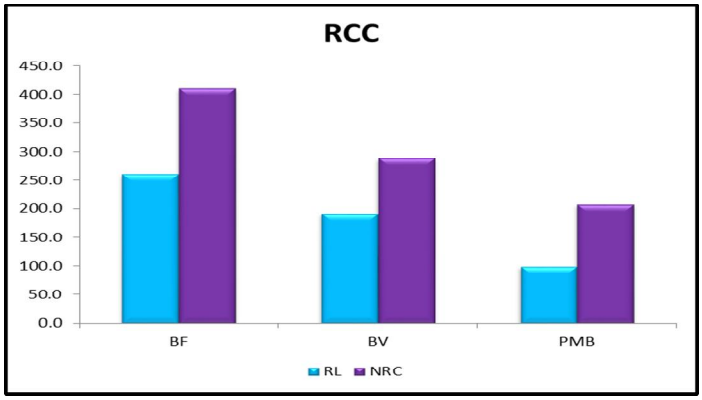


Fig: 7.10.3 Bar diagram showing intralesional mean values of Blood Flow, Blood Volume, Permeability of RCCs in the study group in comparison with normal renal cortex mean values

Paired Samples Test (Renal cell carcinoma vs normal renal cortex)

	Paired Differences					t	Df	Sig. (2-tailed)
	Mean	SD	Std. Error Mean	95% Confidence Interval of the Difference				
				Lower	Upper			
BF-RL – BF-NRC	-149.66	88.17	15.5865	-181.4515	-117.8735	-9.602	31	.000
BV-RL - BV-NRC	-97.66	65.76	11.6252	-121.3692	-73.9496	-8.401	31	.000
PMB-RL - PMB-NRC	-108.38	42.77	7.5601	-123.8002	-92.9623	-14.336	31	.000

Table:7.10.3 Paired samples Test shows significant differences (P<0.01) between the intralesional mean values of Blood Flow, Blood Volume, Permeability of RCCs in the study group in comparison with normal renal cortex mean values

RESULTS OF COMPARISON OF CT PERFUSION PARAMETERS :

Out of the 40 renal lesions among the study group, 32 were RCCs (80%), 5 were Oncocytomas (13%), and 3 were AML with minimal fat(7%). Out of the 32 lesions which were found to be RCC, 21 were clear cell RCC (80%), 6 were chromophobe RCC (19%), 4 were Papillary RCC (12%), 1 was poorly differentiated RCC(3%). And among the clear cell RCC, 11 were of low grade (52%) and 10 were of high grade(48%).

Mean perfusion CT parameter values (BF, BV, PMB) for normal renal cortex and the renal tumours are summarized in the tables and bar charts above. The comparison among the perfusion parameters among various renal lesions and with normal renal cortex showed the below results.

1. It was observed that significant differences existed between Renal cell carcinoma and Oncocytoma in the mean intralesional values of all three parameters (BF, BV, PMB) (P-value <0.01).

2. Angiomyolipoma and Oncocytoma showed significant differences in BV and PMB (with P-Value < 0.01), and differences in BF was found significant only at P-Value < 0.05.

3. No significant differences were seen between AML with minimal fat and RCC (overall) in BF, BV, and PMB values. However, when clear cell RCC and other RCC subtypes were compared with AML separately, significant differences were found in both BF and BV between clear cell RCC and AML (P-Value < 0.01), whereas significant difference was

seen only in BF values between other subtypes of RCC and AML (P-Value < 0.01) and BV values were not significantly different. Again differences in PMB values among AML, clear cell RCC and other RCC subtypes were not statistically significant (P-Value > 0.05).

4. The histopathological subtypes of RCCs namely clear cell type, papillary type and chromophobe type were compared with each other. Mean BF, BV and PMB values were higher in Clear cell RCCs compared to other two subtypes. There were significant differences noted in BF, BV and PMB values between clear cell RCC and papillary RCC (P-Value < 0.01), and also between clear cell RCC and Chromophobe RCC (P-Value < 0.01). No significant differences were seen in BF, BV and PMB between papillary RCC and chromophobe RCC (P-Value > 0.05).

5. Mean intralesional values of BF, BV and PMB obtained from High grade clear cell RCC were compared with that of Low grade clear cell RCC. BF and BV values were found to be significantly higher in High grade RCC (P-Value < 0.01). There were no significant differences in the PMB values between those two groups.

6. The Receiver Operator Characteristic (ROC) curve analysis of the CT perfusion parameters showed the following cut off values in discriminating Renal cell carcinoma from oncocytoma.

a. 366.2 ml/100ml/min for BF with sensitivity of 87.50%, specificity of 100% , PPV of 100% , NPV of 55.56%

b. 254.8 ml/1000ml [or] 25.48 ml/100ml for BV with sensitivity of 81.3%, specificity of 100 % , PPV of 100% and NPV of 45.45%

c. 174.8(0.5ml/100ml/min) [or] 87.4 ml/100ml/min for PMB with sensitivity of 93.8% , specificity of 100% , PPV of 100% and NPV of 71%.

Permeability(PMB) was found to be a better parameter than the remaining two parameters namely, Blood flow(BF) and Blood volume(BV) helpful in differentiating between RCC and oncocytoma.

7. There were significant differences in all the three parameters (BF, BV, PMB) between tumour and normal renal cortex in RCC and AML with minimal fat (P-value < 0.01). Both the groups showed decreased BF, BV, PMB intralesional mean values, compared to the normal renal cortex.

8. However there were no significant differences in the BF, BV, PMB between the intralesional mean values and the normal renal cortex values in the oncocytoma group (P-Value >0.05). Oncocytoma showed similar values within the lesion as that of the normal renal cortex.

Discussion

8. DISCUSSION

Renal cell carcinoma comprises of a group of malignant tumours with different features as well as clinical behaviours, depending on the histopathologic subtype[18,19]. The most aggressive subtype is the clear cell RCC whereas papillary and chromophobe RCC show an indolent behaviour with low metastatic potential. Renal masses also include several benign lesions like oncocytoma and angiomyolipoma, sometimes differentiating them from malignant RCC might be difficult. Also over the recent times, nephron-sparing nephrectomy has showed promising results in early stage RCC, with reduced complication rates and similar survival rates compared to total nephrectomy[34,35]. In this sense, renal lesions characterisation becomes important to recognise a small RCC which can be treated by a partial nephrectomy. Moreover, differentiating benign lesions becomes important in avoiding unnecessary surgery.

Despite the widespread use of multimodality imaging, the characterisation of renal lesion still remains poor in some cases, particularly those of small size < 4 cm[2-4]. Oncocytoma and clear cell RCCs can have similar features and contrast enhancement, posing a challenge in diagnosis[4]. In our study, as previously reported by others[76], we found that both clear cell RCCs and oncocytomas could show two different morphological features, being homogeneously hypervascular (12 and 4 cases, respectively) and hypervascular with a necrotic core (9 and 1 cases, respectively). Also, some

cases of chromophobe RCCs and papillary RCCs, especially hypovascular lesions, had the same CT appearance. For this reason, our study tested the use of CT perfusion which can be added to routine multiphasic CT to help in discriminating between the benign and malignant lesions and their subtypes.

In our study out of the 40 renal lesions, 32 were RCCs (80%), 5 were Oncocytomas (13%), and 3 were AML with minimal fat (7%). Out of the 32 lesions which were found to be RCC, 21 were clear cell RCC (80%), 6 were chromophobe RCC (19%), 4 were Papillary RCC (12%), 1 was poorly differentiated RCC(3%). And among the clear cell RCC, 11 were of low grade (52%) and 10 were of high grade (48%).

The age and gender distribution of renal cell carcinomas and their frequency distribution of subtypes were almost similar to previous studies in literature, whereas oncocytomas were higher in our study (13%) compared to the reported incidence of 3-7%[44-45].

CT perfusion technique allows the quantitative evaluation of tissue perfusion and has shown promising results in the oncologic field[9,76,77]. Our study aimed at evaluating the usefulness of various CT Perfusion Parameters (Blood Flow, Blood Vloume, Permeability) in differentiation and charactersisation of both benign and malignant renal lesions. In our study, ROIs of renal tumour and normal renal cortex were defined manually predominantly concentrating on the most solid portion.

Chen Y et al.[20] reported the mean values obtained from normal renal cortex(BF - 454.32±110.90 mL/min/100g, BV - 23.53 ± 5.71 mL/100g, MTT - 3.62 ± 1.38s, PMB - 63.95 ± 18.85 mL/min/100 g). Several other studies have shown different values of their own. In our study the mean values obtained from normal cortex were 406.78 ± 27.12 mL/min/100ml (BF), 287.9 ± 19.8 mL/1000ml (BV), 206.34 ± 12.75 (0.5 mL/min/100 ml)(PMB). Our results for these parameters were slightly different and cannot be compared as such with the previous studies because of the differences in units, volume analysis, scan protocols, and post-processing algorithms.

It was also demonstrated by **Chen Y et al**[20], that there was a significant difference between BF, BV, and PS of normal renal cortex and RCC and our study results showed the same with significantly reduced BF, BV, PMB mean intralesional values compared to normal renal cortex. (P-Value < 0.01)

Our study showed no significant differences existed between the CT perfusion parameter values between oncocytoma and normal renal cortex which was similar to the study results provided by **Mazzei FG et al.**[76]. These results could be explained by alterations of microvessel architecture in RCC, whereas oncocytomas, instead, appear to exhibit normal architecture, very close to the normal renal cortex.

Also in our study significant differences were seen in all three parameters between RCC and oncocytoma (P-Value <0.01), which differed slightly from the study by **Mazzei FG et al**[76] where only PS and BF values

were found to be statistically different and BV was not significant. The ROC curve analysis was done to find the cut off value, sensitivity, specificity, PPV, NPV. Permeability was found to be the better parameter than the other two (BF, BV) with high sensitivity (93.8%) and specificity (100%) in differentiating RCC from oncocytoma.

AML with minimal fat showed significant differences between intralesional values and normal renal cortex values (P-Value<0.01). No significant differences were seen between AML with minimal fat and RCC (overall) in BF, BV, and PMB values in our study, which was different from the study by **Chen, Chao, et al**.[7] who demonstrated that BV was significantly different between AML with minimal fat and RCC.

Chen, Chao, et al.[7] also found significant difference in BV between AML with minimal fat and clear cell RCC, whereas no significant difference was seen between the Equiv BV, PS, and BF of non-clear cell RCC and AML with minimal fat. Similarly, in our study, clear cell RCC and non-clear cell RCC subtypes were compared with AML with minimal fat separately. In our study significant differences were found in both BF and BV between clear cell RCC and AML (P-Value < 0.01), whereas significant difference was seen only in BF values between non clear cell RCC and AML (P-Value < 0.01). No significant differences were seen in PMB values in AML compared with clear cell RCC and non-clear cell RCC (P-Value > 0.05).

Chen, Chao, et al.[7] also stated that clear cell RCC showed significantly higher BF and BV than papillary RCC and higher BV than chromophobe RCC. **Chen Y et al.**[20] also demonstrated that BF and BV among RCC histologic subtypes were significantly different, whereas MTT and PS were not. Comparable results were also seen in our study. Mean BF, BV and PMB values were significantly higher (P-Value<0.01) in Clear cell RCCs compared to papillary RCC and chromophobe RCC. No significant differences were seen in BF, BV and PMB between papillary RCC and chromophobe RCC (P-Value > 0.05).

Gigli et al.[21] demonstrated that clear cell RCC of different Fuhrman grades had statistically significant differences in perfusion values, as high perfusion indices were associated with high microvessel density. **Zhang YL et al.**[75] also reported that PF(Perfusion Fraction) and BV(Blood volume) values are significantly higher in high-grade CCRCC than in low-grade CCRCC. This was similar to our study, in which we found BF and BV values to be significantly higher in High grade RCC (P-Value < 0.01).

Nevertheless, BF, BV and PMB proved to be the useful diagnostic parameters which can be useful in differentiating benign and malignant renal lesions and their subtypes and provide added information on tumour perfusion.

Limitations of the study

9. LIMITATIONS OF THIS STUDY

However our study had some limitations which are listed below.

1. Out of the total 40 renal lesions, the subgroup of benign lesions included is relatively small(n=8), out of which 5 were oncocytomas and only 3 were AML which might not be an adequate representation for interpretation of the results.

2. Secondly, only 15% of the lesions (n=6) were small renal lesions (<40 mm), which are those with uncertain management, who underwent partial nephrectomy. Rest all were lesions >40 mm who underwent total nephrectomy.

3. This study included only a limited number of papillary and chromophobe RCCs, hence accurate evaluation of these pathologic types was not possible.

4. Furthermore some renal lesions, like transitional cell carcinoma, renal lymphoma are not represented in our case population.

5. Finally the CTp showed some limitations. Patients with breathing difficulties could not be included due to the risk of respiratory artifacts. High radiation dose was another drawback. Protocols that reduce this radiation exposure require further study. Calculating the parameters from a limited tumour section may cause greater measurement variability when tumours tend to be large and heterogeneous. Moreover, as shown

by previous studies, it is not standardised yet, and the values depends on several factors including the hardware platform and software algorithm which might have led to slight differences in results when compared to previous studies in literature.

Conclusion

10. CONCLUSION

CT perfusion is a noninvasive, quantifiable, and feasible technique which allows the quantitative assessment of hemodynamic changes in the lesion.

This study, though it had some limitations, showed the feasibility of CT Perfusion, in discriminating between the malignant renal cell carcinoma from benign renal lesions, especially oncocytoma, which can be an aid in further management.

Preoperative histological knowledge could reduce a number of unnecessary surgeries for benign renal masses and indolent RCCs and also invasive renal mass biopsy could be avoided in some cases.

Significant differences in perfusion parameters among various benign and malignant lesions were apparent in this study. These data may justify the more routine use of this technique in the characterisation, assessment and follow-up of renal lesions especially small and indeterminate ones.

Other potential benefits include identifying tumour histological subtype and predicting potentially aggressive tumours which can help clinicians to better plan the therapy of patients.

Perfusion CT provides complementary information about tumour vascularity and so may act as an in vivo marker of tumour angiogenesis. Thereby it can also be useful in predicting prognosis and tumour response to

various anti angiogenetic therapies at an earlier stage as shown by several studies.

Perfusion CT maps can also be useful for biopsy of very small or indeterminate lesions or large heterogenous lesions, to target the areas of increased BV, to provide a better histologic yield which helps in better response to treatment.

CT Perfusion is an evolving imaging modality and in this recent era concerned with increased interest in active surveillance, more studies in future in CT perfusion will determine whether adding CT perfusion parameters to the routine CT could further refine the predictive ability in the evaluation of renal masses and facilitating targeted therapy.

To conclude, perfusion CT can be readily incorporated into the existing CT protocols, as the combined use of conventional CT and perfusion imaging may contribute to better characterization of renal lesions, which may be difficult on the basis of conventional CT features alone and thus paving way to a better and more targeted approach and management.

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Annexures

ABBREVIATIONS

US	-	Ultrasound
CT	-	Computed Tomography
MDCT	-	Multi Detector Computed Tomography
MRI	-	Magnetic Resonance Imaging
PET	-	Positron Emission Tomography
CTP	-	Perfusion Computed Tomography
RCC	-	Renal Cell Carcinoma
AML	-	Angiomyolipoma
ONCO	-	Oncocytoma
CCRCC	-	Clear Cell Renal Cell Carcinoma
PapRCC	-	Papillary Renal Cell Carcinoma
ChrRCC	-	Chromophobe Renal Cell Carcinoma
ROI	-	Region Of Interest
BV	-	Blood Volume
BF	-	Blood Flow
PS / PMB	-	Permeability Surface area product

MTT	-	Mean Transit Time
MIP	-	Maximum Intensity Projection
HPE	-	Histopathological Examination
n	-	Sample
PPV	-	Positive Predictive Value
NPV	-	Negative Predictive Value
ROC	-	Receiver Operator Characteristic Curve
NRC	-	Normal Renal cortex
LT	-	Left
RT	-	Right
HR	-	Hypervascular
HN	-	Hypervascular with necrosis
HO	-	Hypovascular

PATIENT PROFORMA

STUDY TITLE:

"THE ROLE OF CT PERFUSION IN THE CHARACTERISATION OF SOLITARY RENAL LESIONS - AN ADDED VALUE TO MULTIPHASIC CT"

SI.NO:

NAME:

AGE/SEX:

OCCUPATION:

ADDRESS:

PHONE NO:

PRESENTING COMPLAINTS:

PAST HISTORY:

HYPERTENSION

DIABETES

PREVIOUS H/O RENAL DISEASE;

FAMILY HISTORY :

CLINICAL EXAMINATION:

INVESTIGATIONS:(IF ANY)

ULTRASOUND FINDINGS:

- SIDE/ SITE OF THE LESION
- SINGLE/ MULTIPLE
- SIZE/MARGINS
- ECHOGENICITY
- CYSTIC COMPONENT/ SEPTATIONS
- CALCIFICATION
- AREAS OF NECROSIS
- VASCULARITY
- RENAL VEIN / IVC INVOLVEMENT
- CONTRALATERAL KIDNEY – NORMAL/ABNORMAL

CT FINDINGS:

- SIDE/ SITE OF THE LESION
- SIZE, SHAPE, CONTOUR
- TISSUE CONSISTENCY
- ENHANCEMENT PATTERN
- ANY OTHER SPECIFIC CHARACTERISTICS

CT PERFUSION INTERPRETATION:

Parameters	Within the lesion	Normal renal parenchyma
Blood flow		
Blood volume		
Permeability		

Peak enhancement intensity/ Maximum peak intensity:

INTERPRETATION:

FOLLOW UP:

HPE REPORT:

PATIENT INFORMATION SHEET

We are conducting a study on "**THE ROLE OF CT PERFUSION IN THE CHARACTERISATION OF SOLITARY RENAL LESIONS - AN ADDED VALUE TO MULTIPHASIC CT".** A research is underway at the Madras Medical College on patients with suspected renal lesions on USG/CT.

Patients with suspected renal lesions on USG/CT are evaluated with CT perfusion imaging. CT perfusion parameters are correlated with post-operative histopathology for its usefulness in differentiating the benign & malignant lesions of the kidney and their characterisation, as treatment strategies, prognosis and response to therapy depend on accurate diagnosis.

Your cooperation would be valuable to us for the same.

The privacy of patients in the research will be maintained throughout the study. In the event of publication or presentation your identity will be kept confidential. Taking part in this study is voluntary. You are free to decide whether to participate in this study or to withdraw at anytime.

The result of your study may be intimated to you at the end of the study period or during if anything found abnormal which may aid in management or treatment.

Signature of the investigator Signature of the participant

Dr.S.Swarnalakshmi

Date:

PATIENT INFORMED CONSENT FORM

Title of the study: "THE ROLE OF CT PERFUSION IN THE CHARACTERISATION OF SOLITARY RENAL LESIONS - AN ADDED VALUE TO MULTIPHASIC CT"

Name of the Participant: **Date :**

Age : **Sex :** **Id no:**

1. I have read the information in this form (or it has been read to me).
2. I have read and understood this consent form and the information provided to me.
3. I have had the consent document explained to me.
4. I have been explained about the nature of the study.
5. I have been explained about my rights and responsibilities by the investigator.
6. I have been explained that there are no risks associated with my participation in this study.
7. I am aware of the fact that I can opt out of the study at any time without having to give any reason and this will not affect my future treatment in this hospital.
8. I am also aware that the investigator may terminate my participation in the study at any time, for any reason, without my consent.
9. I hereby give permission to the investigators to release the information obtained from me as result of participation in this study . I understand that they are publicly presented.
10. I have understand that my identity will be kept confidential .
11. I have had my questions answered to my satisfaction.
12. I have decided to be in the research study.
13. By signing this consent form I attest that the information given in this document has been clearly explained to me and understood by me, I will be given a copy of this consent document.

Name **Signature/Thumb impression**

ஆராய்ச்சி தகவல் தாள்

ஆராய்ச்சி தலைப்பு :

சிறுநீரக கட்டியின் தன்மையையும் அதன் வீரியத்தையும் சி.டி. பர்ப்யூசன் ஸ்கேன் மூலம் அதன் இரத்த உள்ளோட்டத்தை வைத்து கணக்கிடுதல்.

மேற்கண்ட ஆராய்ச்சியானது, சென்னை மருத்துவக் கல்லூரியில், அல்ட்ரா சவுண்ட் ஸ்கேன் / சிடி ஸ்கேன் மூலம் கண்டறியப்பட்ட சிறுநீரக கட்டி இருக்கும் நபர்களிடம் மேற்கொள்ளப்படுகிறது.

அல்ட்ரா சவுண்ட் ஸ்கேன் / சிடி ஸ்கேன் மூலம் சிறுநீரக கட்டி இருப்பதாக கண்டறியப்பட்ட நபர்கள், சி.டி. பர்ப்யூசன் ஸ்கேன் எனப்படும் பரிசோதனைக்கு உட்படுத்தப்படுவர். அதன் மூலம் பெறப்படும் துப்புகள், ஊசி /சதை டெஸ்ட் / அறுவை சிகிச்சைக்குப் பின்னர் கட்டியின் திசுத்தன்மைகளோடு ஒப்பிட்டுப்பார்க்கப்படும். இந்த தகவல்கள் சிறுநீரக கட்டியின் தன்மையையும் அதன் வீரியத்தையும்___பற்றி அறிய உதவும். சிறுநீரக கட்டியின் தன்மையையும் மற்றும் அதன் வீரியத்தையும் முன்னரே அறிவதன் மூலம் அதற்கான சிகிச்சை முறைகளையும், சிகிச்சை பலன்களையும் முன் கணிக்க முடியும். தங்களுடைய பங்களிப்பும் ஒத்துழைப்பும் ஆராய்ச்சி நன்முறையில் வெற்றி பெற பெரிதும் உதவியாக அமையும்.

நீங்களும் இந்த ஆராய்ச்சியில் பங்கேற்க நாங்கள் விரும்புகிறோம் . இந்த ஆராய்ச்சியில் உங்களுக்கு பரிசோதனைகள் செய்து அதன் தகவல்களை ஆராய்வோம் .அதனால் தங்களது நோயின் ஆய்வறிக்கையோ அல்லது சிகிச்சையோ பாதிப்பு ஏற்படாது என்பதையும் தெரிவித்துகொள்கிறோம் .

முடிவுகளை அல்லது கருத்துகளை வெளியிடும்போதோ அல்லது ஆராய்ச்சியின் போதோ தங்களது பெயரையோ அல்லது அடையாளங்களையோ வெளியிட மாட்டோம் என்பதையும் தெரிவித்து கொள்கிறோம் .

இந்த ஆராய்ச்சியில் பங்கேற்பது தங்களுடைய விருப்பத்தின் பேரில் தான் இருக்கிறது . மேலும் நீங்கள் எந்நேரமும் இந்த ஆராய்ச்சியிலிருந்து பின்வாங்கலாம் என்பதையும் தெரிவித்துக் கொள்கிறோம் .

இந்த சிறப்பு பரிசோதனையின் முடிவுகளை ஆராய்ச்சியின்போது அல்லது ஆராய்ச்சியின் முடிவின் போது தங்களுக்கு அறிவிக்கப்படும் என்பதையும் தெரிவித்துக் கொள்கிறோம் .

ஆராய்ச்சியாளர் கையொப்பம் பங்கேற்பாளர் கையொப்பம்

நாள் :
இடம் :

ஆராய்ச்சி ஒப்புதல் கடிதம்

ஆராய்ச்சி தலைப்பு :
சிறுநீரக கட்டியின் தன்மையையும் அதன் வீரியத்தையும் சி.டி. பர்ப்யூசன் ஸ்கேன் மூலம் அதன் இரத்த உள்ளோட்டத்தை வைத்து கணக்கிடுதல்.

பெயர் :
வயது :
பாலினம் :

இந்த ஆய்வு , சி.டி. பர்ப்யூசன் ஸ்கேன் மூலம், சிறுநீரக கட்டியின் இரத்த உள்ளோட்டத்தை வைத்து , அதன் தன்மையையும் மற்றும் அதன் வீரியத்தையும் அறுவை சிகிச்சைக்குப் முன்னரே அறிய உதவும் என்பதை அறிவேன் .

இந்த ஆராய்ச்சியின் விவரங்களும் அதன் நோக்கங்களும் முழுமையாக எனக்கு தெளிவாக விளக்கப்பட்டது . எனக்கு விளக்கப்பட்ட விஷயங்களை நான் புரிந்துகொண்டு எனது சம்மதத்தை தெரிவிக்கிறேன் .

இந்த ஆராய்ச்சியில் பிறரின் நிர்பந்தமின்றி என் சொந்த விருப்பத்தின்பேரில் பங்கு பெறுகின்றேன் .

நான் என்னுடைய சுய நினைவுடனும் மற்றும் முழு சுதந்திரத்துடனும் இந்த மருத்துவ ஆராய்ச்சியில் என்னை சேர்த்துக்கொள்ள சம்மதிக்கிறேன் .

தேதி : **பங்கேற்பாளர் கையொப்பம்**

MASTER CHART

S.No	Name	Age	Sex	Size (mean lesion diameter) (cm)	Side	Location	CT characteristics	Renal lesion				Normal renal cortex				Histopathological Diagnosis
								MIP (HU) - lesion	Blood Flow(BF) ml/100ml/min	Blood Volume (BV) ml/1000ml	Permeability (PMB) 0.5ml/100ml/min	MIP (HU) - NRC	Blood Flow (BF) ml/100ml/min	Blood Volume (BV) ml/1000ml	Permeability (PMB) 0.5 ml/100ml/min	
1	Vijaya	40	F	6.5	Left	Mid	Hypervascular with necrosis	148.9	339	229.3	86.2	167.8	404.9	258.2	194.2	Clear cell Renal cell carcinoma - High Grade
2	VijayaKumari	36	F	5.1	Left	Mid	Hypervascular	153.9	284.8	203.7	162.3	159.1	410.5	290.3	208.3	Clear cell Renal cell carcinoma - Low Grade
3	Sangeetha	59	F	5.4	Left	Lower Pole	Hypervascular	149.2	248.1	198.4	91	163.8	355.2	273.1	200.1	Clear cell Renal cell carcinoma - Low Grade
4	Hussain Beevi	39	F	1.8	Left	Upper Pole	Hypovascular	99.5	239.7	133.4	88.1	168.5	377.8	260.7	194.1	Angiomyolipoma with minimal fat
5	Abdul Rahman	71	M	4.3	Right	Mid	Hypervascular	161.7	261.8	206.3	120.6	165.8	384.6	289.3	194.3	Clear cell Renal cell carcinoma - Low Grade
6	Rajalakshmi	63	F	4.9	Left	Lower Pole	Hypovascular	97.2	165.3	107.9	47.1	170.4	428.4	296.4	172.6	Chromophobe Renal cell carcinoma
7	Arumugam	37	M	2.2	Left	Mid	Hypervascular	175.2	382.3	261.3	232.1	169	387	260.5	211.9	Oncocytoma
8	Shanmugam	50	M	11.8	Left	Mid	Hypervascular with necrosis	140.6	284.2	211.9	80.4	167.6	421.6	297.5	217.4	Poorly differentiated Adenocarcinoma
9	Sivagami	65	F	8.7	Left	Mid	Hypervascular with necrosis	136	159.4	103.5	54.5	169.1	418.3	284.7	232.5	Chromophobe Renal cell carcinoma
10	Suriya Begum	62	F	3.6	Right	Upper Pole	Hypervascular	171.4	408	326.9	202.1	164	430.3	316.9	200.3	Oncocytoma
11	Gunasekaran	55	M	11.2	Right	Lower Pole	Hypervascular with necrosis	152.9	328.4	243.8	150.2	172	404.7	281.9	198.4	Clear cell Renal cell carcinoma - High Grade
12	Murugan	68	M	10.9	Right	Mid	Hypervascular	150.2	351.8	264.2	93.2	169.3	435.2	311.4	211.6	Clear cell Renal cell carcinoma - High Grade
13	Palani	61	M	6.2	Left	Mid	Hypervascular	144.1	282	209.9	101.5	169.9	417.1	284.6	220.1	Clear cell Renal cell carcinoma - Low Grade
14	Inbamani	64	F	6.1	Left	Mid	Hypovascular	67.1	90	81.2	53.5	164.8	380.7	321.1	200.1	Papillary renal cell carcinoma
15	Kathalingam	64	M	5.9	Right	Lower Pole	Hypervascular	169.5	431.5	312.8	219.3	158.2	386.1	293.9	209.2	Oncocytoma
16	John Arputham	53	M	4.3	Right	Lower Pole	Hypovascular	110.3	147.5	97.3	57.2	166.8	374.7	249.1	213.4	Chromophobe Renal cell carcinoma
17	Elavazhagan	51	M	5.5	Left	Lower Pole	Hypervascular	146.3	378.4	270.3	176.2	161.9	436.9	299.2	211.9	Clear cell Renal cell carcinoma - High Grade
18	Chandra	37	F	4.2	Left	Mid	Hypervascular	143.7	232.8	119.6	86.3	159.7	348.4	243.9	198.3	Angiomyolipoma with minimal fat
19	Sargunam	70	F	3.5	Left	Lower Pole	Hypervascular with necrosis	140.7	380.2	268.3	169.3	153.9	468	330.1	189.4	Clear cell Renal cell carcinoma - Low Grade
20	Selvam	57	M	7.2	Left	Upper Pole	Hypervascular with necrosis	142.4	328.4	237.6	93.2	163.7	399.5	278.7	206.4	Clear cell Renal cell carcinoma - High Grade
21	Vellayan	43	M	3.6	Right	Mid	Hypovascular	54.9	99.8	76.4	69.2	170.2	402.8	280.9	224.7	Papillary renal cell carcinoma
22	Sevandhiappan	58	M	4.6	Left	Upper Pole	Hypervascular	159.3	297.1	205.3	98.4	169.6	438.1	289.6	215.7	Clear cell Renal cell carcinoma - Low Grade
23	Muthupandi	59	M	8.2	Right	Mid	Hypervascular with necrosis	163.2	375.7	262.4	175.4	157.8	397.5	295.3	205	Oncocytoma
24	Bargavi	53	F	7.7	Left	Lower Pole	Hypervascular with necrosis	152.9	338.1	248.3	93.1	165.4	417.4	287.2	202.5	Clear cell Renal cell carcinoma - High Grade
25	Manjula	56	F	4.9	Left	Upper Pole	Hypovascular	72.1	164.3	113.4	67.2	159.9	434.7	301.7	230.3	Papillary renal cell carcinoma
26	Rangappan	73	M	6.4	Left	Lower Pole	Hypervascular	147.2	377.2	197.2	100.1	158.3	376.9	269.8	217.8	Clear cell Renal cell carcinoma - Low Grade
27	Nagomi	42	F	3.6	Left	Lower Pole	Hypovascular	102.8	251.7	136.2	73.2	169.3	392.5	276.7	184.3	Angiomyolipoma with minimal fat
28	Alagesan	54	M	5.7	Right	Mid	Hypervascular	153.7	383.2	281.4	179.6	164.3	458	323.9	221.9	Clear cell Renal cell carcinoma - High Grade
29	Sekar	54	M	5.8	Left	Mid	Hypervascular with necrosis	141.7	278.1	207.2	93.2	162.8	405.6	282.6	204.6	Clear cell Renal cell carcinoma - Low Grade
30	Kothandapani	61	M	5.8	Right	Upper Pole	Hypovascular	98.4	169.4	119.3	83.2	157.4	420.8	297.3	214.8	Chromophobe Renal cell carcinoma
31	Sumathi	53	F	4.1	Left	Mid	Hypervascular	147.2	265.3	201.3	136.8	161.9	375.9	282.2	201.1	Clear cell Renal cell carcinoma - Low Grade
32	Nagavalli	68	F	6.4	Left	Upper Pole	Hypervascular	178.3	426.1	325.7	188.5	158.6	419.5	328.5	198.4	Oncocytoma
33	Thirumurthy	63	M	6.9	Left	Mid	Hypovascular	101.4	160.3	143.2	58.2	165.5	419.4	291.7	205.8	Chromophobe Renal cell carcinoma
34	Kanniyappan	60	M	5.3	Right	Upper Pole	Hypervascular	142.6	283.1	266.2	174.2	158.9	424.6	289.8	213.8	Clear cell Renal cell carcinoma - Low Grade
35	Mariyammal	55	F	8.7	Left	Mid	Hypervascular with necrosis	151.9	302.1	239.2	88.2	162.2	375.8	273.3	193.2	Clear cell Renal cell carcinoma - High Grade
36	Govardhanan	68	M	4.4	Right	Mid	Hypovascular	66.3	106.4	84.5	40.6	169.5	422.1	294	209.1	Papillary renal cell carcinoma
37	Chellamuthu	67	M	9.1	Right	Mid	Hypervascular	147.2	356.7	268.4	139.8	163.3	443.6	301.7	228.3	Clear cell Renal cell carcinoma - High Grade
38	Duraikannu	51	M	4.7	Left	Mid	Hypervascular	140.2	161.2	103.6	50.6	160.9	412.6	285.6	208.2	Chromophobe Renal cell carcinoma
39	Rathinam	52	M	6.5	Left	Upper Pole	Hypervascular with necrosis	152.8	308.1	232.3	79.2	173.6	367.2	268.6	189.3	Clear cell Renal cell carcinoma - High Grade
40	Chakrapani	61	M	7.6	Right	Lower Pole	Hypervascular with necrosis	149.3	263.4	197.3	96	167.4	396.5	277.7	200.4	Clear cell Renal cell carcinoma - Low Grade

ETHICS COMMITTEE APPROVAL LETTER

INSTITUTIONAL ETHICS COMMITTEE
MADRAS MEDICAL COLLEGE, CHENNAI 600 003

EC Reg.No.ECR/270/Inst./TN/2013
Telephone No.044 25305301A
Fax: 011 25363970

CERTIFICATE OF APPROVAL

To
Dr.S.Swarna Lakshmi
Post Graduate in Radio Diagnosis
Madras Medical College
Chennai

Dear Dr.S.Swarna Lakshmi,

The Institutional Ethics Committee has considered your request and approved your study titled **"THE ROLE OF CT PERFUSION IN THE CHARACTERISATION OF SOLITARY RENAL LESIONS – AN ADDED VALUE TO MULTIPHASIC CT " NO. 18012017.**

The following members of Ethics Committee were present in the meeting hold on **03.01.2017** conducted at Madras Medical College, Chennai 3

1.Dr.C.Rajendran, MD.,	:Chairperson
2.Dr.M.K.Muralidharan,MS.,M.Ch.,Dean, MMC,Ch-3	:Deputy Chairperson
3.Prof.Sudha Seshayyan,MD., Vice Principal,MMC,Ch-3	: Member Secretary
4.Prof.B.Vasanthi,MD., Prof.of Pharmacology.,MMC,Ch-3	: Member
5.Prof.A.Rajendran,MS, Prof. of Surgery,MMC,Ch-3	: Member
6.Prof.N.Gopalakrishnan,MD,Director,Inst.of Nephrology,MMC,Ch	: Member
7.Prof.Baby Vasumathi,MD.,Director, Inst. of O & G	: Member
8.Prof.K.Ramadevi,MD.,Director,Inst.of Bio-Che,MMC,Ch-3	: Member
9.Prof.R.Padmavathy, MD, Director,Inst.of Pathology,MMC,Ch-3	: Member
10.Prof.S.Mayilvahanan,MD,Director, Inst. of Int.Med,MMC, Ch-3	: Member
11.Tmt.J.Rajalakshmi, JAO,MMC, Ch-3	: Lay Person
12.Thiru S.Govindasamy, BA.,BL,High Court,Chennai	: Lawyer
13.Tmt.Arnold Saulina, MA.,MSW.,	:Social Scientist

We approve the proposal to be conducted in its presented form.

The Institutional Ethics Committee expects to be informed about the progress of the study and SAE occurring in the course of the study, any changes in the protocol and patients information/informed consent and asks to be provided a copy of the final report.

Member Secretary – Ethics Committee

MEMBER SECRETARY
INSTITUTIONAL ETHICS COMMITTEE
MADRAS MEDICAL COLLEGE
CHENNAI-600 003

PLAGIARISM ANALYSIS REPORT

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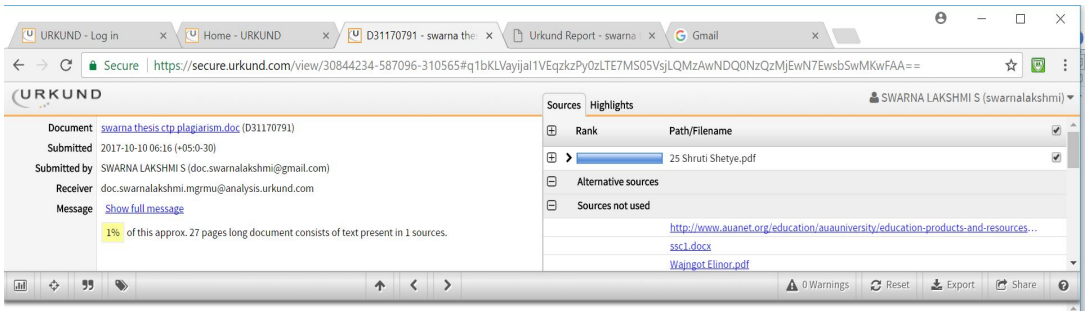

"THE ROLE OF CT PERFUSION IN THE CHARACTERISATION OF SOLITARY RENAL LESIONS – AN ADDED VALUE TO MULTIPHASIC CT"

1. INTRODUCTION

Majority of the renal lesions are found incidentally by routine ultrasound examination. And in recent times, the diagnosis of renal masses have increased, because of the widespread use of computed tomography (CT), and magnetic resonance (MR) imaging.

Most of the lesions turn out to be simple renal cysts which can be diagnosed easily and they do not require any treatment. However, solid and complex cystic renal masses are also found, and most of them are clearly malignant which needs prompt surgical removal, although some may be benign and surgery may not be needed in such cases.

Thereby, the proper characterisation of the renal masses is needed for appropriate management and helps in deciding the need for surgery.

There have been many studies focussing on the imaging features and degree of enhancement on multiphasic, multidetector CT or MRI as a means of distinguishing benign and malignant renal lesions and also there have been reports of subtype differentiation of renal cell carcinomas by CT or

"THE ROLE OF CT PERFUSION IN THE CHARACTERISATION OF SOLITARY RENAL LESIONS – AN ADDED VALUE TO MULTIPHASIC CT"

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There have been many studies focussing on the imaging features and degree of enhancement on multiphasic, multidetector CT or MRI as a means of distinguishing benign and malignant renal lesions and also there have been reports of subtype differentiation of renal cell carcinomas by CT or MRI[1,2,3].

Although the great value of imaging for detection of renal lesions has increased in recent years, the accuracy rate on preoperative characterisation of their nature remains low[4]. Percutaneous biopsy could be a useful tool in dubious cases, but it is an invasive approach[5,6].

Recently, computed tomography perfusion (CTp), a functional tool which allows a quantitative evaluation of tissue perfusion through consecutive scans acquired during contrast media injection, showed promising results in the oncologic field, even in renal lesion characterisation[7] and further aids in subtyping of renal cell carcinomas.

Perfusion CT is based on the temporal changes in tissue attenuation after intravenous administration of iodinated contrast media. Tissue iodine concentration determines enhancement and is an indirect reflection of tissue vascularity and vascular physiology[8,9]. These are predicted based on certain perfusion parameters, namely blood flow (BF), blood volume (BV), mean transit time (MTT) and permeability (PMB).

2. RATIONALE OF THE STUDY

Most of the renal tumours (almost ninety percent) come under five histologic categories: clear cell carcinoma (or conventional carcinoma), which is the most common, chromophobe carcinoma, papillary carcinoma, and two common benign tumours, namely angiomyolipoma and Oncocytoma [10].

Angiomyolipoma (AML) is a common benign tumour of the kidney and presence of intratumoral fat allows accurate identification by imaging.[11,12] But, in cases of AML with minimal fat, intratumoral fat cannot be visualized in an AML on routine imaging[13-15]. And they resemble renal cell carcinoma (RCC), leading to surgery unnecessarily. Also differentiating between oncocytoma and renal cell carcinoma represents a diagnostic challenge[4].

Renal cell carcinomas (RCC) account for 80–90% of all renal neoplasms,[1,2,16] with multiple subtypes that differ in their histopathologic features, genetic expression pattern, and clinical behaviour. Among the renal cell carcinomas, Clear cell RCC, papillary RCC, and chromophobe RCC are the most representative subtypes, accounting to 65–70%, 15–20%, and 6–11% of RCCs, respectively[3,17].

PLAGIARISM CERTIFICATE

This is to certify that this dissertation work titled **"THE ROLE OF CT PERFUSION IN THE CHARACTERISATION OF SOLITARY RENAL LESIONS - AN ADDED VALUE TO MULTIPHASIC CT"** of the candidate **Dr.SWARNALAKSHMI.S** with registration Number **201518004** for the award of **M.D RADIODIAGNOSIS** in the branch of **VIII**. I personally verified the urkund .com website for the purpose of plagiarism check. I found that the uploaded thesis file contains from introduction to conclusion pages and result shows **1 percentage** of plagiarism in the dissertation.

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